DISEASES of the CHEST

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Surgical Removal of the Carotid Body for Bronchial Asthma

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Introduction

Because of the existence of a wide variety of implied etiologic factors and obscurity concerning its pathogenesis, a definitive form of therapy for bronchial asthma has not been forthcoming. Surgical treatment[1,7,14] has been predicted on a presumed imbalance of autonomic nervous system function. Kümmell,[6,7] in 1923, advocated resection of the superior cervical sympathetic ganglion, but Horner's syndrome and parotid pain were frequent distressing complications. In 1924, Kappis[4,5] assumed a predominant parasympathetic role and sectioned the vagus nerve. Short term results with both procedures were encouraging, but a complete cure was rare beyond three years.[2,11,12,14] Göbell[3] combined both of these procedures and in 1928 he performed bilateral superior cervical ganglionectomy and severed the right vagus nerve. The results[12,13] were no better than for either procedure alone and the combined operation was attended by a significantly increased mortality rate. Carotid body excision, first reported by the author in 1942,[8] is a simple and often effective method of treatment. Residual symptoms and operative mortality are negligible.

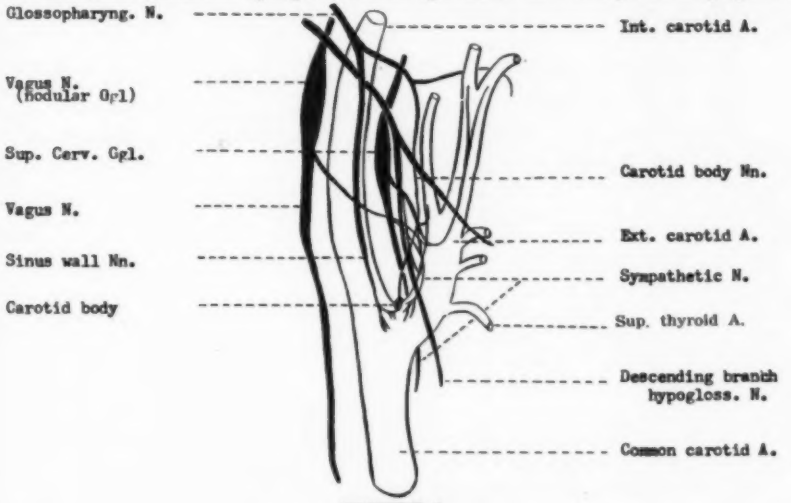

FIGURE 1

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This paper describes some of the physiologic studies conducted in an attempt to elucidate the function of the carotid body and its associated innervations. The indications for and the results of this procedure are also presented with a physiologic explanation for its efficacy based on experience with approximately 3900 cases.

Anatomic Considerations[3]

The carotid body is a rice-grain-sized structure located at the carotid bifurcation (Fig. 1). Microscopically it consists of a capsule and connective tissue septae which divide the parenchymal cells into lobules. On hematoxylin eosin staining, there are two types of parenchymal cells, viz., those with light staining cytoplasm and oval or elliptical nuclei, and those with darkly staining cytoplasm and smaller nuclei containing reticulum in a pattern similar to that of plasma cells. There are medullated and non-medullated nerve fibers present, but no free nerve endings in the true sense are seen. There are both filter-like and sinusoidal vascular patterns suggesting a specific sensory organ function.

Gross anatomic relations are illustrated in Fig. 1. The carotid body artery arises directly from the carotid artery. The nerve supply is in the form of plexuses which are quite separate and distinct. There are cranial parasympathetic and thoracic sympathetic contributions to these. The sinus wall nerve constitutes a plexus descending along the anterior surface of the internal carotid artery; this terminates at the lateral aspect of the bifurcation. This plexus contains glosso-pharyngeal and probably vagus fibers. A more medially placed plexus is termed the carotid body nerve. This plexus also contains glossopharyngeal fibers, and along with periarterial fibers from the superior cervical ganlglion, it constitutes the predominant nerve supply to the carotid body. Functional aspects of this anatomy, based on experiments to be described, are presented graphically in Fig. 2.

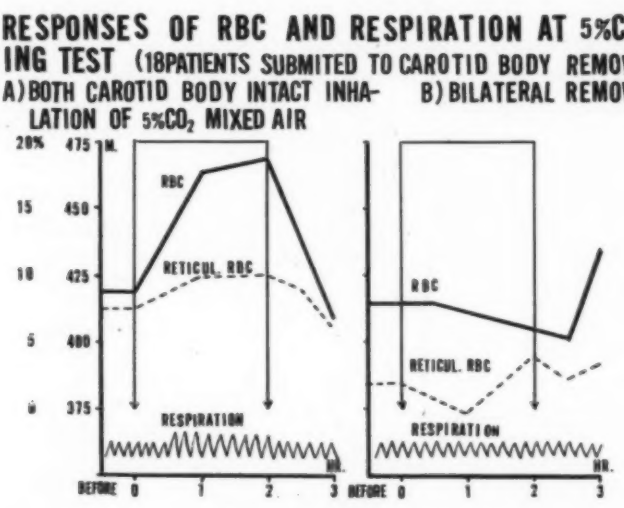

FIGURE 3

Physiologic Investigations

The carotid body contains both mechanical pressor-receptors and chemoreceptors which reflexly influence both respiratory function and blood pressure. A variety of pharmacologic studies employing CO_2 inhalation, lobeline, sodium cyanide and local anesthetics have been carried out in rabbits and humans[9,10] in an attempt to elucidate further the functional pathways from the carotid body. These pharmacologic studies also have been supplemented by electro-physiologic and histologic studies.

The four following experiments were undertaken first to define the role of the carotid body receptors in the overall reflex arc of influence on respiratory function and regulation of blood pressure.

1. A CO_2 loading test was performed before and after carotid body removal in humans. Prior to removal, 5 per cent CO_2 inhalation resulted in an increase in the red blood cell mass. Following unilateral removal of the carotid body there was little change in these responses to 5 per cent CO_2 inhalation. However, bilateral removal abolished these responses of the internal respiratory mechanism completely (Fig. 3).

2. A 0.4 mg. dose of sodium cyanide, given intravenously, was noted to elevate blood pressure approximately 15 mm. Hg while the same dose of lobeline resulted in a 20 mm. Hg drop in blood pressure. Unilateral carotid body removal did not significantly change these responses, whereas bilateral removal completely abolished them; the latter effects were permanent when the bilateral removal was complete. When sodium cyanide (0.6 mg.) was injected into the carotid artery itself on the operated side, however, these responses did not occur if the removal of the gland

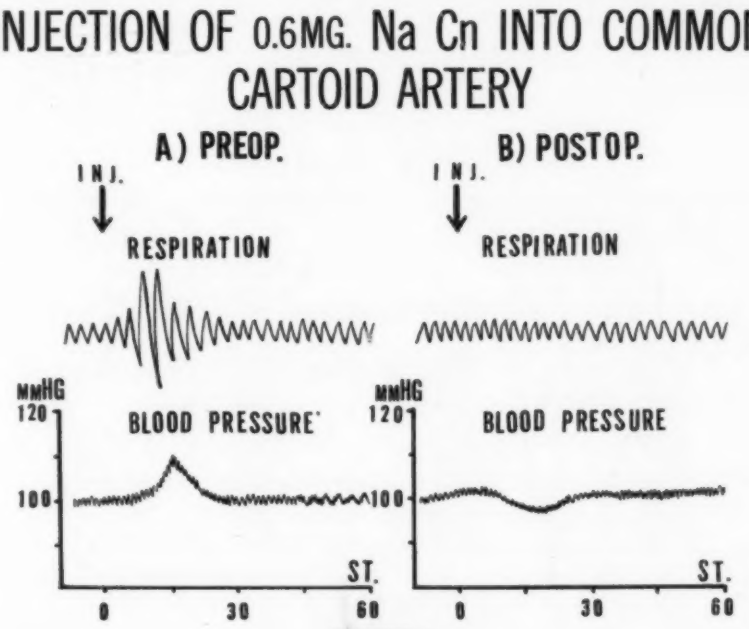

FIGURE 4

has been completed. This is available as a test whether the removal of this gland is complete or not (Fig. 4).

3 Lobeline (0.1 mg.) was injected into different loci of the carotid periarterial plexus and the respiratory responses were recorded; respiration was increased in both rate and depth. The most significant changes were noted on injection of the area around the carotid gody and in the common carotid artery wall proximal to the origin of its blood supply (Fig. 5). Control injections of the femoral plexus failed to produce such changes. Repeated injections of the carotid body area after removal failed to produce these changes.

4. Sodium cyanide (0.1 cc. in a 1 per cent solution) was noted to increase the rate and depth of respirations also; this amount was injected into these same areas. The responses were noted to be maximal when injection was into the carotid body itself and somewhat less maximal with injection into the carotid artery. When injected into the carotid sympathetic plexus, there was no change noted.

These four experiments are taken to indicate the presence, within the carotid body, of chemoreceptors which are an integral part of the reflex arcs influencing respiratory and blood pressure functions. These receptors have been shown to function either to intravascular or to direct intracarotid body stimulation. There is also a suggestion that chemoreceptors within the carotid body may also influence red blood cell mass. Having thus demonstrated the presence of these receptors within the carotid body, studies were then done to determine what, if any, specific roles the sinus wall nerve plexus and the carotid body nerve plexus play.

5. The sinus wall nerve was exposed and severed; lobeline and sodium cyanide were given intravenously as in experiment 2 above. Under these circumstances, the reflex changes in blood pressure were absent, but the respiratory reflex changes remained intact. Following this, division of the carotid body nerves was carried out and this resulted in the abolition of reflex respiratory changes to the intravenous administration of these

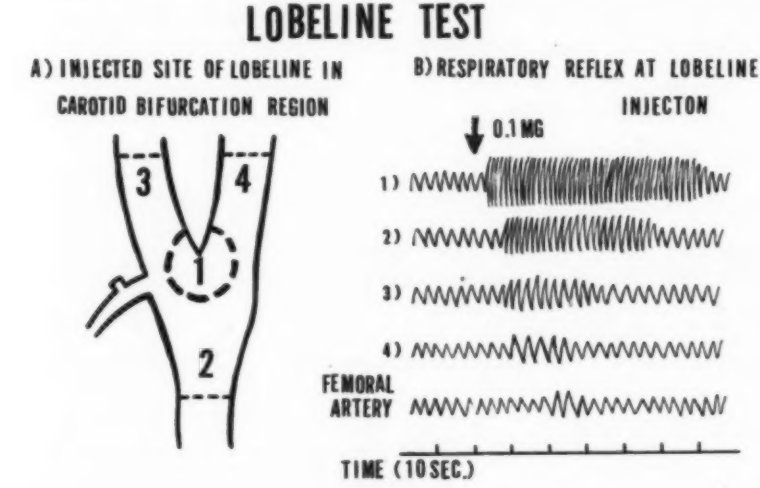

FIGURE 5

agents. This study indicates that blood pressure changes are mediated primarily via the sinus wall nerve plexus while respiratory changes are mediated primarily by the carotid body nerve plexus. Such a different role between these two conduction systems is further illustrated by recordings of changes in electrical potentials recorded from these nerves as responses to different stimuli.

6. Carotid artery occlusion resulted in disappearance of rhythmical centripetal impulses from the sinus wall nerve, which are normally synchronized with the pulse, and in elevation of the blood pressure. Removal of the occlusion is followed by reversion to a normal blood pressure and resumption of a rhythmical pulse and centripetal currents. It is felt, therefore, that blood pressure control is through the sinus wall nerves and that the carotid body may function to keep blood pressure levels down under normal circumstances. On the other hand, sporadic centripetal impulses recorded from the carotid body nerves, unrelated to that from the sinus wall nerve, may be shown to be rapidly augmented by suffocation and reduced by hyperventilation.

Finally, the following observations indicate a relationship between carotid body function and the autonomic nervous system; whether the sympathetic nerve fibers arise in or are shunted through the carotid body is not certain.

7. It has been noted that injections of small doses of local anesthetics into the carotid body were followed by an increase in the red blood cell count. This change was without effect on the blood pressure or respiratory reflexes. This may be a reflection of the fact that sympathetic fibers are more sensitive to local anesthetics than are cranial nerve fibers. Furthermore, injections of local anesthetics into these areas in patients are often followed by alleviation of autonomic discomfort such as feeling

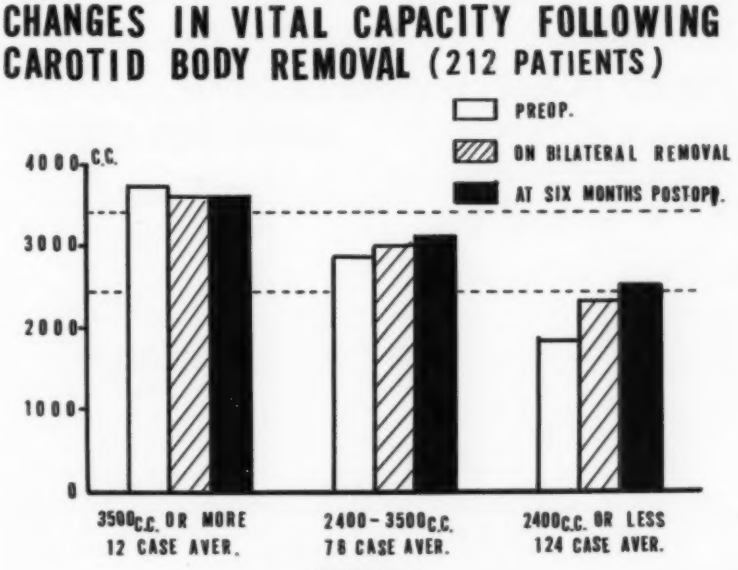

FIGURE 6

of suffocation in bronchial asthma and the postprandial symptoms which often follow gastrointestinal surgery. Similar effects also have been reproduced by removal of the carotid body, division of fibers from the superior cervical ganglion or ganglionectomy, *per se*. However, it is the author's experience that in this respect removal of the carotid body gives more persistent effects than ganglionectomy alone. It has also been shown[10] by histologic tracing of degenerated nerve fibers that carotid body removal results in an extensive but systematic degeneration of centripetal fibers originating in this gland as well as in the central nervous system. It was noted also in studies of rabbits decerebrated at various levels that the red blood cell regulating center is located in the thalamus and that it is markedly inactivated by removal of the carotid body.

These studies demonstrate the role of this gland as a receptor organ for chemical and physical changes in the character of the blood flow peripherally and as a relay in the reflex control of blood pressure and respiratory functions.

Observations on Carotid Body Removal in Patients

The respiratory rates have been little influenced, but in those patients with an extremely low preoperative vital capacity, there is often an increase in vital capacity following unilateral removal of the gland. There is only a slight further increase following bilateral removal (Fig. 5). A noticeable increase in the respiratory movements of the diaphragm is usually seen. These changes have been accompanied by an increase in arterial oxygen saturation.

With regard to cardiovascular function, normotensive blood pressure levels change very little when surgical intervention is limited to the gland itself. However, with only a six-month follow-up, hypertensive patients have been noted to have a significant drop in blood pressure

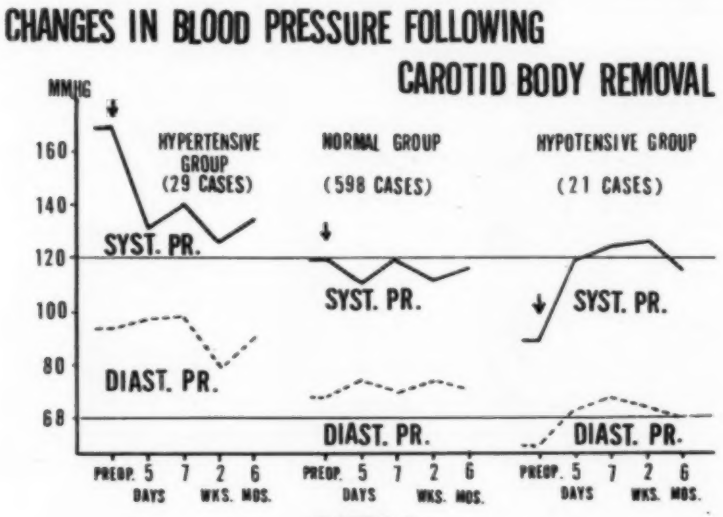

FIGURE 7

while those with hypotensive preoperative levels have shown an elevation in blood pressure (Fig. 7). In some patients with hypertension there has been subsidence of optic disc edema. Electrocardiographic changes have been noted also (Fig. 8), and a transitory shortening of the circulation time has been observed. A transitory increase in red blood cell mass has been noted as well (Fig. 9).

There has been an increase in serum adrenalin levels lasting for approximately three weeks, associated with proliferation of adrenal chromophilic cells. Perhaps, related to this has been an improvement of initially abnormal responses to adrenalin or pilocarpine tests for a certain time.

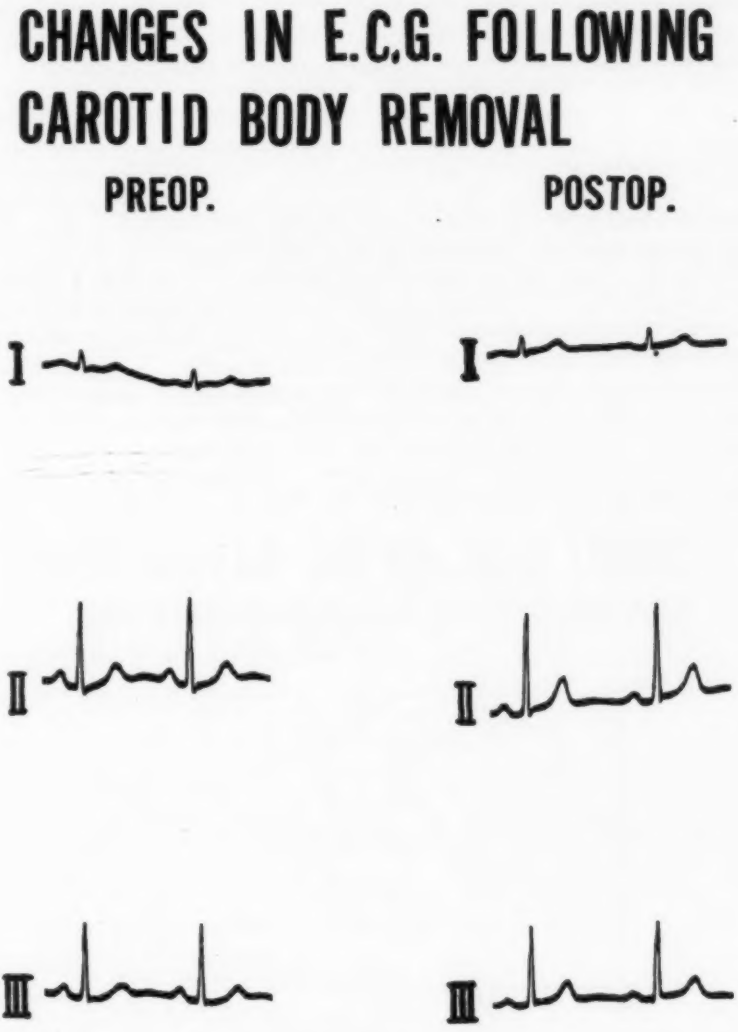

FIGURE 8

In many instances there were improvements in the manifestations of allergies and gastric peristalsis patterns, perhaps related to the increased adrenalin levels.

Operative Indications, Technique and Results

In many of the cases described below the indication for surgery was empirical. For better therapeutic results an attempt must be made to select the patients on the basis of clinical features and laboratory evaluation. On review of the series it appeared that this procedure is not contraindicated in patients with a family history of bronchial asthma (Table 1) or in patients with proved allergy (Table 2). These results indicate that the procedure may be effective in many asthmatics with proved allergens as initiators of attacks. As a rule, superior cervical ganglionectomy has been disappointing in these patients. Patients with accompanying tuberculosis or with other evidence of pulmonary pathology, or mediastinitis, have not had good results (Table 3). This also holds for patients with x-ray evidence of cardiac disease, such as an enlarged heart. Attempts have been made to determine by preoperative testing which patients will have a good result. Responses to atropine, adrenalin and pilocarpine have been of little value in this respect. However, an increase in vital capacity had been observed in many successfully treated cases; and it was then noted that this procedure might be promising if a marked increase in the vital capacity occurred with inhalation of 20 cc. of diluted hydrochloric acid (1 drop of concentrated hydrochloric acid to 20 cc. of water) (Table 4).

Operative technique is standard. The skin incision is made along the anterior border of the sternocleido-mastoid muscle starting 1.5 cm. below the base of the ear and extending for 5 cm. This muscle is dissected free at its anterior border and clamped by two hemostats for retraction. The bifurcation of the carotid artery is exposed by blunt dissection. Then

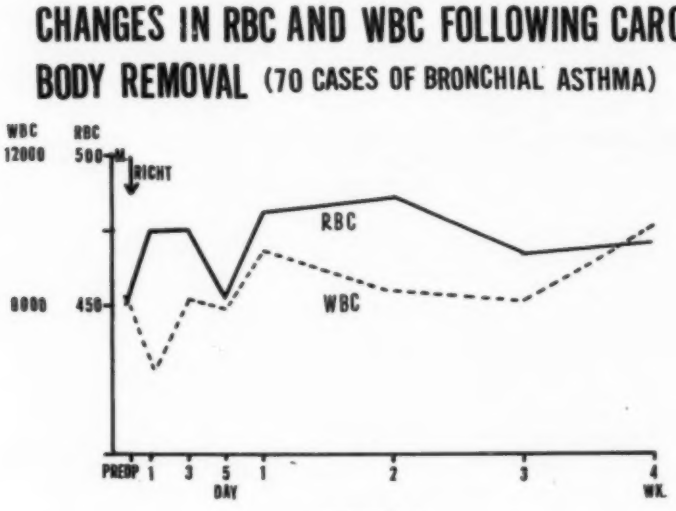

FIGURE 9

the adventitial wall of the external carotid artery is held at the origin of the superior thyroid artery and retracted laterally. The inner aspect of the bifurcation is exposed and the carotid body is seen as a small whitish mass at the bifurcation near the external carotid artery. The carotid body is dissected free from the adventitial wall of the external carotid artery, and the carotid body artery is ligated at its origin and is divided from the bifurcation. This operative technique allows us to remove the carotid body alone, avoiding unnecessary injury to surrounding nerves nad vessels.

Using this technique, a total series of 3,914 cases were operated upon in Japan at various institutions to March, 1949. (This survey includes 1013 cases of my own series during the same period.) Of these, 2,535 cases have shown moderate to marked improvement. A relatively similar improvement scale has been shown in a recent survey on my own series too as described in Table 5. (This survey has been made on the basis of the exact answer alone to the questionnaires sent by us.) Namely, in terms of percentage, 81.3 per cent showed cure or improvement six months after surgery, 72.6 per cent showed good results at two years and 58 per cent still had good results after five years. Sixteen per cent have had no postoperative episodes. Operative results of bilateral removal are comparable with those of unilateral removal at six months or later (Table 6). Thus, it would appear that removal of the contralateral carotid body has little further effect in those patients in whom unilateral removal of this gland has not been beneficial. Of course, this assumes equal bilateral pathology. Good results are predominantly found in those patients who showed increased vital capacity (Table 7).

Discussion

Knowledge of the presence of the carotid body dates back to Haller's description of the carotid body in 1743.* It is now believed that this organ perceives certain chemical stimuli in the blood stream, as well as mechanical stimuli associated with changes in the dynamics of circulation, and conveys these as impulses through its centripetal fibers which are specific for individual stimuli. In addition, this gland can receive impulses from the autonomic nervous system.

Critique of Kümmell's operation of superior cervical ganglionectomy[2,4,5,14] has been directed at the vagueness of its logical basis since the vagus nerve has been believed to play the primary role in the mechanism of bronchial asthma. Notwithstanding, surgery of the vagus nerve has been rather uniformly disappointing.[5] It was Glaser's[1] assumption that centripetal sympathetic fibers convey chest pain or discomfort at the onset of this disease. Actually, since the true pathogenesis of this disease has not been completely elucidated as yet, no perfectly logical interpretation can be made. It has been generally accepted that autonomic pain or discomfort is almost exclusively of sympathetic origin. Though largely empirical at the onset, many of our studies support Glaser's assumption. In addition, we have successfully demonstrated the sympathetic centripetal fibers for red blood cell regulation. Kümmell's operation evidently comprises severence of these fibers; that is, of the conduction tract for experiencing autonomic discomfort and regulating red blood cell mass (internal respiration). The ganglionectomy, however, results in severence of the centrifugal fibers too, which is thought to account for the postoperative sequelae of his operation. Removal of the carotid body severs not only the centripetal sympathetic fibers aforementioned, but also those fibers which control depth and rate of respiration (external respiration). This would reduce to a much greater extent, the excitability of the respiratory center as well as the autonomic centers both of which are beneficial to patients with bronchial asthma. Removal of the carotid body, *per se*, does not necessitate severence of the centrifugal sympathetic fibers, thereby obviating such untoward sequelae as often

*History of Surgery of Carotid Body

Haller	1743	discovery of carotid body
Jacobovici	1928	resection of sinus wall nerve for epilepsy
Danielopolu	1931	same as above
Nakayama	1942	removal of carotid body for bronchial asthma and Buerger's disease

follows superior cervical ganglionectomy. Complete removal of this gland, however, does create noncompensatory results. This would be accordant with the fact that the therapeutic effect of carotid body extirpation is permanent in many cases, whereas following Kümmell's operation, severed fibers recommunicate with each other in a few months.

SUMMARY AND CONCLUSIONS

Removal of the carotid body is often the procedure of choice in asthmatic patients. This is a simple procedure and shows good results without residual ill-effects in many cases. Indications for this operation must be better defined and strictly considered. Its logical basis, operative technique, indications, immediate and long-term results are described on the basis of the author's wide experiences.

RESUMEN

La extirpación del cuerpo carotídeo a menudo es el procedimiento de elección en los asmáticos. Es un procedimiento sencillo que da buenos resultados sin efectos residuales en muchos casos.

Las indicaciones para este procedimiento deben ser mejor definidas y estrictamente consideradas. Su base lógica, la técnica operatoria, las indicaciones y los resultados inmediatos y tardíos se describen basándose en la amplia experiencia del autor.

RESUMÉ

L'exérèse du corpuscule carotidien est souvent le procédé de choix chez les malades atteints d'asthme. C'est une méthode simple et qui donne dans beaucoup de cas de bons résultats sans suitès facheuses. Les indications de cette méthode doivent être mieux définies et envisagées avec précision. L'auteur décrit la base logique, la technique opératoire, les indications, les résultats immédiats et lointains de cette technique en l'appuyant sur sa grande expérience personnelle.

ZUSAMMENFASSUNG

Die Entfernung des Glomus craoticum ist bei asthmatischen Patienten häufig die Methode der Wahl. Sie ist einfach und hat gute Ergebnisse. In vielen Fällen verschwinden die Krankheitserscheinungen rückfallsfrei. Die Indikation zu dem Eingriff muss besser festgelegt und streng berücksichtigt werden. Die Grundlagen der Methode, die operative Technik, Indikation, Sofort- und Langzeitergebnisse werden aufgrund umfangreicher Untersuchungen des Autors beschrieben.

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Glomectomy for Asthma

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The plight of intractable asthmatics is often directed to the attention of the thoracic surgeon. The fault is mechanical, for there is an obstruction, be it organic or functional. Such sufferers struggle to move air freely, either in or out of air tubes. Often surgeons are asked for advice regarding bronchial toilet (bronchoscopy, tracheotomy), correction of organic defects which trigger generalized bronchospasm (hidden bronchiectasis), or to help with mechanical aids (respirators).

In addition to assisting in the management of patients in status asthmaticus, surgeons have concerned themselves with methods to control bronchospasm in chronic cases by nerve interruption. Cervical or intrathoracic severance of sympathetic or vagal fibers has been used for almost 40 years. The author, in a paper on pulmonary denervation, presented to the American College of Allergists in April of 1958, included a detailed historical resume.** Professor Komei Nakayama has referred to the early history of surgical attempts to relieve asthmatics in the account of his experiences which appears in this issue.

In 1957, Dr. Yaemon Shiraha, from Osaka, joined our Clinic for postgraduate study and training. From him, we were pleased to learn of Professor Nakayama's work. Direct correspondence and a review of results, published in the Japanese literature, were encouraging. Benefits seemed significant and untoward sequelae of the procedure non-existent.

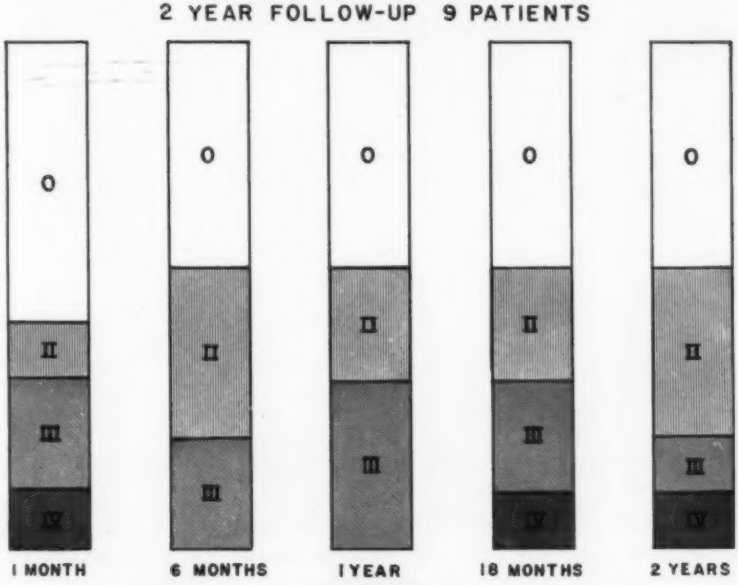

FIGURE 1

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**_Annals of Allergy_, 17:534, 1959.

Clinical Experience

Since May of 1958, 69 cases of intractable asthma have been selected at the Overholt Thoracic Clinic for treatment by glomectomy. None had responded favorably to conservative therapy and all were considered medical failures.†

By eliminating one case lost to follow-up and 16 recent cases, we have information on 52 patients in whom the post-operative period has been from six months to over two years. It was difficult to evaluate the degree of benefit. However, reports from referring physicians and patients, together with follow-up examinations, have permitted a reasonable judgment. Response has been graded in five categories as follows:

Category	Improvement	Attacks	Drugs
IV	Marked	None	None or occasional
III	Significant	Rare	Less or occasional
II	Moderate	Occasional	Less
I	Slight	Fewer	Some
0	None	No change	Some

In Figure 1 is recorded the appraisal of benefits in nine patients who have been followed for over two years. In five of them, some improvement

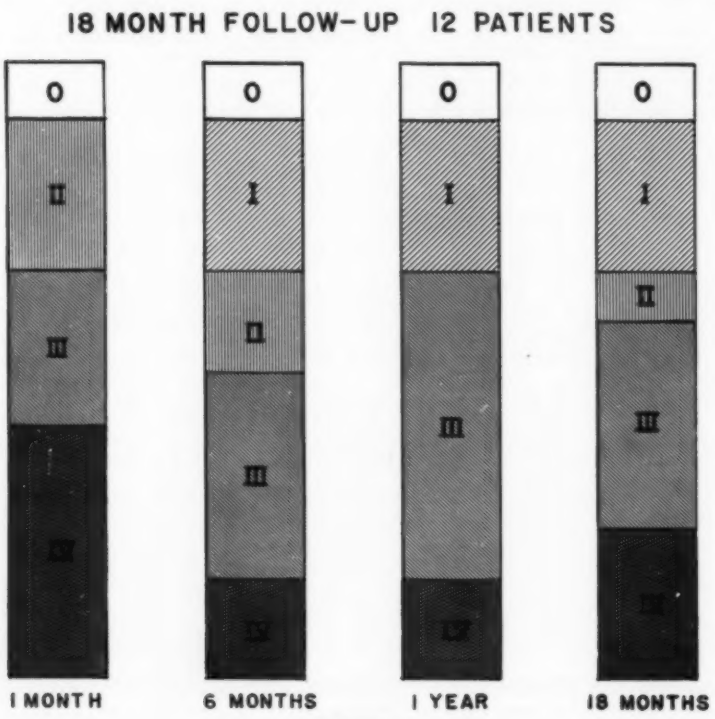

FIGURE 2

†Previous medication included bronchodilators and expectorants, desensitization, changes in climate, psychotherapy and electric shock, intermittent positive pressure breathing, aerosols, bronchoscopic aspiration, and steroid therapy.

was noted. In Figures 2, 3, and 4 are shown the results in 12, 18, and 13 patients which were followed for 18, 12, and six months, respectively. In these latter groups, benefits were obtained in a higher percentage of cases. This, we believe, is due to a better selection of patients.

In addition to the 69 cases treated primarily for intractable asthma, there were five pulmonary cripples with emphysema in whom there was a significant element of bronchospasm and for whom glomectomy was carried out. The results are listed individually for them in Table 1.

Technique

A thorough knowledge of the surgical anatomy of the area and the employment of a meticulous dissection permits the execution of the procedure without risk. A period of two to three days in the hospital is sufficient.

The operation is carried out under local anesthesia. Pre-operative medication is hardly required, but usually a barbiturate, with or without meperidin (Demerol), is given 30 to 40 minutes in advance. A two-inch incision is placed in a crease line in the neck, one-third of the distance between the angle of the mandible and clavicle. The platysma muscle is divided and the sternocleidomastoid retracted laterally. The dissection is carried down to the carotid sheath exposing the bifurcation. The superior thyroid artery is ligated and divided near its take-off in order to facilitate rotation of the carotid bulb and expose the medial aspect of the bifurcation. The carotid body is about the size of a grain of rice

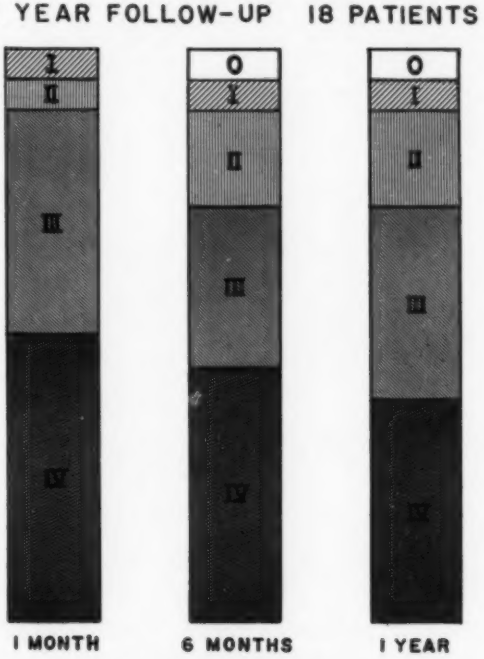

FIGURE 3

and is hidden within the adventitia of the vessel and is of the same color. The perivascular adventitia is removed from one centimeter above to one centimeter below the bifurcation. This severs connections of the nerve plexus which surrounds the carotid body. The dissection of the adventitia is necessary in order to locate and identify the body. It is usually located exactly at the point of bifurcation on its medial aspect. Rarely, it may be found either in the center of the crotch or on the lateral wall. The small artery entering the carotid body is clamped, divided, and ligated. The upper stalk of tissue above the carotid body is then clamped, divided, and ligated.*

Comment

Approximately four out of five asthmatic patients, in whom no structural abnormality of the bronchial system was suspected or demonstrated, have been improved by this simple and innocuous procedure. There has been no untoward physiologic disturbance. Alterations in blood pressure and pulse rate have not been observed and there have been no vasomotor disturbances. Comparative spirometric measurements, before and after, have been difficult to evaluate. The intensity of bronchospasm varies greatly from minute to minute, and hour to hour. Timed vital capacity was improved in those reporting symptomatic relief. Many patients reported marked betterment in breathing ability. However, rales persisted and the expiratory phase continued to be prolonged. Apparently, relief of bronchospasm is not the major contribution of glomectomy. The benefit observed is better explained by chemical alterations of arterial blood with associated influences on respiratory rate. The carotid body is a chemoreceptor, sensitive to: (1) hypoxemia, (2) decreased pH, and (3) CO_2 retention. Each carotid body is a relay station between the lung and brain, and alterations in the blood are first registered there. Stimulation causes hyperpnea. This is beneficial when the airways are clear and ventilation adequate. In the asthmatic, however, broncho-

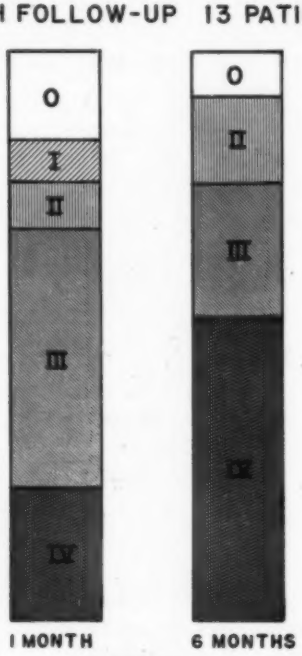

FIGURE 4

*In two of the surgical specimens, the pathologist failed to identify a carotid body in the matrix of nerve tissue.

TABLE 1

		1 Mo.	6 Mos.	1 Yr.	18 Mos.	2 Yrs.
Mr. M. 55	Emphysema Fenestration Unilat. Bronchiectasis	III	I	0	0	0
Miss B. 58	Emphysema Tussic Syncope Bilat. Bronchiectasis	III	II	II	IV	IV
Miss F. 63	Emphysema Cough	II	II	III	III	III
Mr. L. 57	Emphysema Cor Pulmonale	III	III	III	III	III
Mr. D. 67	Emphysema Lt. Bronchiectasis	0	II	III	III	

0=no improvement; I=slight improvement; II=moderate improvement; III=significant improvement; IV=marked improvement

spasm and the accumulation of secretions have already interfered with airway patency and ventilation. Tachypnea, with attendant shallow ventilation, then does not improve oxygenation of blood. Actually, the increase in unventilated lung volume may reduce blood oxygenation to cause further stimulus for tachypnea. Removal of the carotid body may break this vicious cycle in the asthmatic.

SUMMARY

In the past three years, 69 patients with intractable asthma have been selected for treatment by glomectomy at the Overholt Thoracic Clinic. Some benefit was found in four out of five patients. Over half were improved to a marked or significant degree. These clinical results parallel closely those reported by Nakayama.

The carotid body is a chemoreceptor, sensitive to: (1) hypoxemia, (2) decreased pH, and (3) CO_2 retention. Stimulation causes hyperpnea. This is beneficial if airways are clear. In the asthmatic, such a reflex initiates a vicious cycle. An already diminished functional capacity, due to bronchospasm, mucosal swelling, and secretion accumulation, is further reduced by hyperpnea. Removal of one carotid body apparently prevents such an unwanted sequence, as well as partially interrupts pathways of communication to the pulmonary plexus which contains bronchodilator fibers.

RESUMEN

En los pasados tres años se escogieron 69 enfermos con asma intratable para ser tratados con glomectomía en la Clinica Torácica de Overholt.

Algún beneficio se obtuvo en cuatro de cada cinco enfermos. Más de la mitad mejoran en un grado marcado o significante.

Estos resultados clínicos son paralelos a los relatados por Nakayama.

El cuerpo carotídeo es quimioreceptor, sensible a: (1) anoxemia, (2) pH disminuido y (3) retención de CO_2. La estimulación del él produce hiperpnea.

Esto es benéfico si las vias aereas estan libres. En el asmático tal reflejo inicia un círculo vicioso. Con una capacidad funcional ya disminuida debido al broncoespasmo, hinchazon de la mucosa y acúmulo de secreciones, se reduce mas por la hiperpnea. La extirpación de un cuerpo carotídeo aparentemente evita esta indeseable secuencia asi como interrumpe parcialmente las vías de comunicación hacia el plexopulmonar que continen fibras broncodilatadoras.

RESUMÉ

Dans les trois dernières années, 69 malades atteint d'asthme intraitable ont été selectionnés pour un traitement par glomectomie à la "Overholt Thoracic Clinic."

Une certaine amélioration fut notée chez 4 ou 5 malades. Plus de la moitié a ressenti une amélioration très nette.

Ces résultats se rapprochent de très près de ceux donnés par Nakayama.

Le corpuscule carotidien est un recepteur chimique sensible (1) à l'anorexia, (2) à la diminution du pH (3) à la rétention de CO_2. La stimulation provoque de hyperpnéa. Elle est bénéfique si les voies respiratoires sont libres. Chez l'asthmatique un tel reflexe engendre un cercle vicieux. La capacité fonctionnelle déja réduite par le spasme bronchique, par l'inflammation des muqueuses ou l'accumulation de sécrétion l'est encore davantage par l'hyperpnéa. L'exérèse d'un corpuscule carotidien prévient apparemment une série d'inconvénients si indésirables et interrompt partiellement la voie de communication vers le plexus pulmonaire qui contient les fibres bronchodilatatrices.

ZUSAMMENFASSUNG

In den vergangenen drei Jahren wurden an der Overholt'schen Thoraxklinik 69 Patienten mit behandlungsrefraktärem Asthma ausgewählt zur Therapie mittels Drüsenexstirpation. Eine leichte Besserung ergab sich bei 4 von 5 Patienten. Mehr als die Hälfte wurden wesentlich bezw. signifikant gebessert. Diese klinischen Ergebnisse entsprachen weitgehend denjenigen, die von Nakayama mitgeteilt worden sind.

Die Carotis-Drüse ist ein Chemoreceptor, der empfindlich ist auf: (1) Anoxämie, (2) herabgesetztes pH, und (3) CO_2-Retension. Eine Reizung verursacht Hyperpnoe. Dies ist günstig, wenn die Luftwege frei sind. Bei dem Asthmakranken veranlaßt ein solcher Reflex einen Circulus vitiosus. Eine bereits herabgesetzte Lungenfunktion infolge Bronchospasmus, Schleimhautschwellung und Sekretbildung wird durch eine Hyperpnoe weiter vermindert. Die Entfernung eines Carotis Drüsen-korpers verhindert augenscheinlich solche unerwünschten Folgen und unterbricht teilweise die Verbindungswege zum Plexus pulmonaris, der bronchodilatatorische Fasern enthält.

CRICOTHYROID MEMBRANE BRONCHOGRAPHY

A transcricoid needle puncture technic was used by the authors for bronchography in 85 cases. The frequency and seriousness of the complications of this procedure appear to have been exaggerated in the past. With absorbable contrast media, antibiotic control, and careful attention to asepsis, the method appears to be safe, effective and time-saving. It is particularly suited for departments of radiology in large and busy general hospitals.

Hemley, S. D., Arida, E. J., Diggs, A. M., and Freeman, S. L.: "Percutaneous Cricothyroid Membrane Bronchography," *Radiol.*, 76:763, 1961.

RADIOLOGIC CHANGES IN PULMONARY VENOUS HYPERTENSION, WITH SPECIAL REFERENCE TO THE ROOT SHADOWS AND LOBULAR PATTERN

Venous, mixed and arterial varieties of pulmonary hypertension are defined. Pulmonary venous hypertension is a state in which the pressure in the pulmonary venous system is high, while the pulmonary vascular resistance remains normal or increases only slightly, and any rise in pulmonary arterial pressure is passive. The root shadows are of venous type and loss of translucency and opacification of the interlobular septa are likely to be present, especially when the patient is active. Dilatation of the vessels to the upper zone is common, but constriction of these to the lower zone is not seen.

Pulmonary mixed hypertension occurs when a raised pulmonary vascular resistance, of spastic or structural origin, complicates pulmonary venous hypertension to produce a disproportionate rise in the pulmonary arterial pressure. The root shadows are of arterial type. Lower zonal constriction is often present and contrasts with the dilatation of the vessels in the upper zone. Opacification of the interlobular septa is often seen, but loss of translucency in the lower zone tends to be less obvious than in pulmonary venous hypertension.

Pulmonary arterial hypertension occurs whenever a raised pulmonary arterial pressure occurs without obstruction to pulmonary venous drainage. The radiologic changes vary with the underlying cause, but the features of a raised pulmonary venous pressure are absent, constriction of peripheral vessels is not zonal, and the root shadows are of arterial type.

Opacification of the interlobular septa causes horizontal lines and a lobular pattern on the radiogram. This opacification may be due to edema, when it is reversible, or to structural changes, when it is irreversible.

Harley, H. R. S.: "The Radiological Changes in Pulmonary Venous Hypertension, with Special Reference to the Root Shadows and Lobular Pattern," *Brit. Heart J.*, 23:75, 1961.

Atypical Forms of M. tuberculosis*

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I must preface this paper with the statement that only the most elementary facts and the most important names can be given in a discussion that involves some of the most intricate technical procedures of science. This problem concerns principles of biology, bacteriology, heredity and biochemistry.

After Koch discovered the tubercle bacillus, he, along with Cohnheim and others, looked upon the bacillus as a rather rigid and unchanging micro-organism. In fact, he headed a group termed monomorphists. It was not long, however, before reports were made of branching forms by Metchnikoff, and later, fine granular forms by Spengler and several granular types by Much. In the meantime, in 1892 Maffucci described the avian strain, and Theobald Smith the bovine strain in 1896. Various saprophytic acid-fast bacilli were found in a great variety of places as well as many acid-fast strains that infected cold blooded animals. These discoveries began to show that there may be variations in tubercle bacilli that were not suspected by the discoverer.

The discoveries of variation had only begun. In 1921, Corper[1] found three strains out of 100, which he isolated from sputum, did not infect guinea pigs. Griffith[2] in England isolated bacilli from skin lesions that were about midway between the human and avian strains in behavior. Petroff[3] separated BCG into two types on culture plates—the rough or avirulent form and the smooth or virulent form. DeKruif[4] called this phenomenon "dissociation." A short time after this and extending over a period of more than 20 years I had the opportunity to observe changes in a tremendously large material. These observations anticipated many of the findings that have been described later, including chromogens, phage-like activity, L-forms of bacilli and some of the acid-fast or partially acid-fast granular forms described by Much. In this material there was perhaps some contamination, but no more so than was inherent in the methods of that day. There were many observations that, in the light of recent bacteriologic finding, deserve a re-examination.

There were at least three cultures out of approximately 50,000 that corresponded to what has been reported recently by general bacteriologists as the L-forms.[5,6] Two of these specimens grew microscopic colonies that contained very small bacilli, approximately one-tenth of the normal size and upon transplanting, these bacilli became larger and by the third transplant they were normal in appearance and activity. In other cultures, granular forms appeared and the growth of these granules into bacilli was unique. Some sprouted into small bacilli directly, others were comma shaped, while others grew out like doughnuts and finally broke at one point producing at first horseshoe-shaped forms and later they straightened out into bacilli.

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*Read in part before the Polish Medical Society, Warsaw, Poland, September 12, 1960.
**Missouri State Sanatorium.

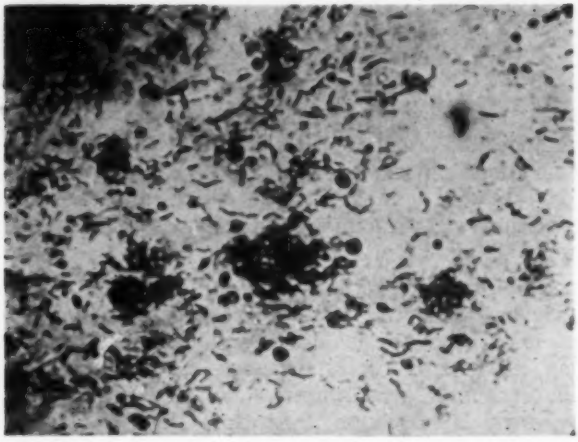

FIGURE 1: Microphotograph of a smear of an A. F. strain of a microcolony on cream-egg medium. Note the small dots enlarging to the size of red blood cells and shaped like doughnuts. The rim of the doughnut breaks and releases a regular curved bacillus that finally straightens out. x 1200

Perhaps one of the most interesting cultures among many that produced variable types of growth and staining was one obtained from a mass of retroperitoneal lymph nodes of Hodgkin's disease.[7-10] There were large numbers of acid-fast bacilli throughout these nodes. On culturing these bacilli in the usual manner there were at least four different types of bacillary growth. One was what we considered a typical tubercle bacillus. Another started out to grow as a typical form, but on removal from the incubator, it turned a tawny brown which corresponds today to the photochromogen, but became lysed in a few days to a soft, avian-like culture suggesting a phage process. Another had all the appearance of an avian form of colony and acid-fast bacillus although it was not virulent for chickens. The fourth form was a mixture of nonacid-fast and granular bacilli with a few acid-fast forms interspersed in a soft, slimy growth on the surface of the media. Only the first strain showed any virulence for guinea pigs. The avian-like form would be considered a Runyon Type III.

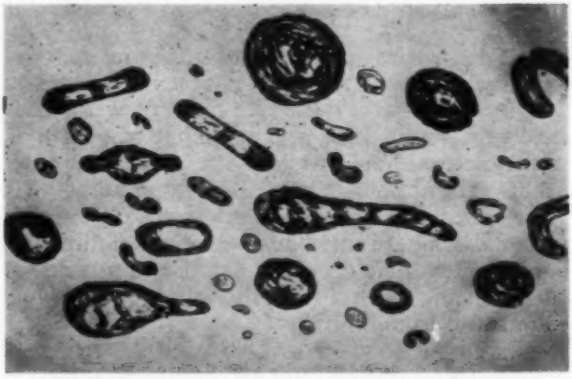

FIGURE 2: A sketch of the various froms observed.

Another similar case was obtained from the lymph nodes of a patient with bovine tuberculosis. In this heterogeneous mixture there were many acid-fast granules. Some of the colonies were soft and smooth like avian, others more like typical bovine bacilli.

Still another specimen was obtained from a localized area of caseous pneumonia in the upper lobe of a patient dying of pulmonary tuberculosis. This area was about 10 cm. across, and on smearing revealed innumerable granular forms with huge granules mostly in the center of the bacilli. On culturing these forms directly, there was an overgrowth of a Staphylococcus-like organism that was arranged in tetrads. Most of these tetrads failed to grow beyond the third transplant. Some of these tetrads still maintained partial acid-fastness indicating the possibility that they had arisen from the huge granules. In attempting to prove this point single cells were picked by a Peterfie micromanipulator and cultivated on culture media. There was only one growth out of many attempts, and this was typical of *M. tuberculosis* in every way. The limitations of equipment and technique prevented the establishment of the true nature of these granular bacilli.

Many other bacteriologists of the older school have reported a great number of variations from the usual type.

Within the last few years, several bacteriologists have observed minute forms from different bacteria which as yet have not been entirely explained. It is possible that these small forms as applied to the tubercle bacillus were what was described as L-forms and may have been responsible for the "filterability" of the tubercle bacillus as described by Fontes in 1910.[11] Another feature of these small forms was considered by Mellon[12] and Kahn[13] for tubercle bacilli and by Hadley[14] for enteric bacilli as life cycle forms of these respective organisms, but in a critical review of the subject by Braun,[15] a life cycle theory was shown to be untenable.

Although very much of that which has been cited represented random observations in different parts of the world, much of it has not been accepted; however, there has been a new light thrown on this whole field as a result of two most important events.

The first was the discovery of the various antimicrobial drugs beginning with Domagk's classical work on the sulfas and continuing on through the many antimicrobials that have been discovered since that time including the equally classical work of Fleming, Lehmann, Waksman, and others. The second is the impact of new discoveries in the fields of genetics, bacteriology, biochemistry and microbic heredity.

Antimicrobial drugs soon began to produce resistant forms among the micro-organisms which at first were suppressed by the drugs. The various cocci were soon found to develop resistance to sulfa drugs. After antibiotics were discovered, resistance in practically all bacteria was found to develop against the antibiotics as they appeared. The phenomenon of resistance caused a new view to develop in the whole field of antimircobial therapy. It has brought into play the second great phenomenon mentioned above, the sciences of genetics, bacteriology, and biochemistry. These, in turn, emphasized the importance of mutation which has become accepted, not only as the principal cause of changes of life on the earth in the past, but also many changes in bacteria at the present time.

While the findings of bacteriologists regarding what has been called transmutation, transduction, re-combination, etc., are most interesting phenomena, it seems unlikely that such can be applied to anything but unicellular organisms. Even in bacteria the role of mutation probably plays the dominant role.

It might be helpful to give a brief review of the development within the science of biology and heredity. We all are familiar with the development of the Theory of Evolution. Although a very old theory, it was really crystalized by the immortal work of Darwin during the middle of the 19th century. His dictum of "survival of the fittest through natural selection" has been one of the most famous declarations in the field of science. Just how these changes take place, however, were not clear at that time because Lamarck's theory of acquired characteristics still had many advocates. Not until DeVries advanced the theory of mutation in the latter part of the 19th century did the theory of Darwin take on more meaning. One of the first to suggest mutation of bacteria was Beijerinck[16] in 1901 who suggested that the changes in colony formation may be due to mutation. It was followed by a vast number of bacteriologists who began to appreciate the significance and meaning of mutation and the changes that take place in micro-organisms. Not until the last 15 or 20 years, however, has the problem become so clear that mutation is now considered as the principal cause of changes not only in macro, but also in microscopic forms of life. Some of the leaders in the sciences mentioned are Muller[17] in genetics on the drosophila fruit fly, J. Lederberg[18] on *E. coli* and other bacteria in the field of bacteriology and Tatum and many other biochemists[20] in the chemistry of heredity. Although these men have not explained everything, the door has been opened so that we are beginning to see some of the most subtle secrets of nature at work.

The hypothetical genes, the determiners of structural growth and functional characteristics of any living thing, are made up of ribose or desoxyribose, joined with phosphorus and four or five amino acids to form ribonucleic acid — RNA — or desoxyribonucleic acid — DNA. These

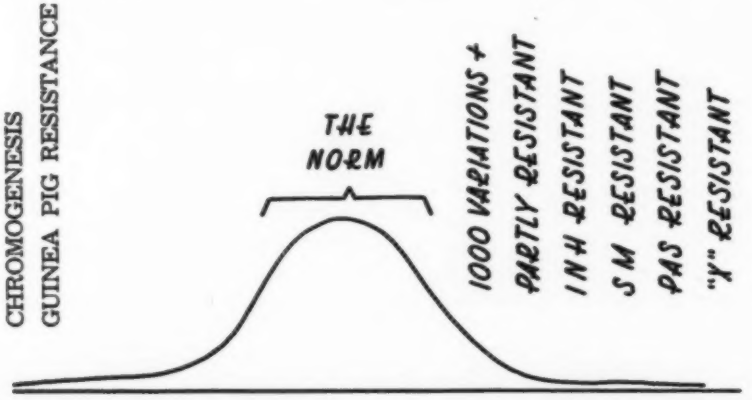

FIGURE 3: A hypothetical sketch of the growth population of tubercle bacilli, showing the great mass of more normal cells and the various resistant forms in decreasing numbers towards the periphery. The central mass is suppressed by the various drugs, leaving the few resistant forms to replace the normals.

chemicals have been shown by both biochemical methods and the Watson-Crick[21] x-ray diffraction technique to consist of a flat ribbon-like structure arranged around a helix in millions of coils. On each side of the ribbon is a row of ribonucleic acid or desoxynucleic acid with the amino acid groups in the center and the ribose or desoxyribose and phosphoric groups along the edge of the ribbon. This rather simple arrangement does not seem enough to explain all the changes in heredity, but when it is realized that there are millions of these groups in one giant molecule and that there are millions of genes, the complexity of the whole mechanism is better realized. The arrangement of these groups seems to determine the genetic characteristics of the individual.

Normally this complex giant molecule is surprisingly stable. During normal cell division, the ribbon-like structure reproduces itself exactly by splitting lengthwise into two equal parts. There is no precision in the knowledge of man to surpass this, and each of the two equal parts in some manner acts as catalysts to direct the building of a new cell exactly like the original.

If this complex chemical were completely stable, however, no change would ever have taken place in living things, and there probably would be no life on the earth. As it is, with all its precision, the process is subject to some variation. Spontaneous changes whose cause we do not fully understand yet, take place in the genetic structure. Not only are new mutants different in some ways, but changes in the genetic structure itself are perpetuated.

The cause of this mutation, which is said to be constant for every species against every antagonist, is unknown, but cosmic rays and various influences of heat and cold are thought to play a role. Certain things have been proved, however, to alter the rate of mutations; for example, x-ray and radium radiation and chemicals have greatly speeded up mutational changes. There is also every reason to believe that antibiotics and antimicrobials in general may also increase the rate of mutation.

With this background we can approach the problem of atypical and resistant forms of tubercle bacilli with a better understanding. We can now begin to appreciate better the significance of resistance of bacteria to drugs.

Under ordinary circumstances the normal forms of bacteria vastly outnumber the variant or mutant forms in any population and will outgrow them. This is easy to understand since the mutation occurs only once in many thousands to millions of organisms. However, a mutant, if for any reason becomes better adapted to grow than the normal form like becoming more resistant to human defences, may outgrow the normal form (Fig. 3). This may account for the many atypical forms that have been found associated with tuberculous disease. They have been called "anonymous" bacilli by Marks and Trollope,[22] "atypical" by McMillen and Kushner,[23] "unclassified" by Hartwig, *et al.*[24] They have been classified as photochromogens, scotochromogens, and non-chromogen by Runyon[25] as groups I, II, and III respectively. A fourth group of rapid growers has been added since. It is obvious that this grouping is a tenuous one because new variants are rapidly appearing. Many have

been found to be associated in granulomatous disease similar to or identical with what we have always called tuberculosis.

Among many others, Buhler and Pollak[26] in Kansas City reported 17 cases called tuberculosis from which "yellow" bacilli were obtained. Crow and associates[27] in Georgia found atypical bacilli, afterwards called the "Battey" bacillus, which came from tuberculosis-like lesions of the lung. Lewis[28] and associates in Florida; Lester around Chicago,[29] Young[30] in England and many others have proved that the atypical forms can cause, or at least seem to be the predominant parasitic agent in the tuberculosis-like ulcerative lesions of the lung.

Most of these atypical infections are considered to be spontaneous and independent of treatment, but they may well be a result of the action of the drugs on the bacilli. The incidence is somewhere between 3 and 10 per cent. In one year's analysis we found it be 5.6 per cent with virulent forms making up about 4 per cent.

With regard to resistant forms, it is difficult to draw a line between simple resistance and many of the non-chromogenic atypical forms. Resistant forms in most respects may still behave like typical tubercle bacilli, but when they lose their virulence for guinea pigs, the lines become tenuous.

In the case of the drug-resistant forms, the factor of natural selection is clearly seen. These mutants which are resistant to a given drug thrive in its presence as the normal counterparts are destroyed, and a drug like isoniazid acts upon tubercle bacilli for the first time so that the great mass of normal cells are affected and growth is stopped. The antibiotic seems to act like a key that locks the door to growth, but the mutant, once in a 100,000 or more cells, soon outgrows the other cells because the key will not unlock the chemical lock, and the mutant is able to develop and soon take over all growth.

Whether the drugs actually affect the genetic structure and speed up the formation of mutants is still a question which deserves more study. In any case, the result of drug therapy has been to increase the finding of drug resistant mutants in the tuberculosis population.

One of the first indications of mutation-affecting drug treatment was the appearance of resistance to streptomycin after a few weeks treatment, then resistance was found to para-aminosalicylic acid and after isoniazid was discovered, it was even found to produce resistance more rapidly than either of the other two. In addition, many of the bacilli resistant to INH were found by many workers to be avirulent or only partially virulent for guinea pigs.

Cohn, Middlebrook, and Russell[31] have determined the frequency of mutation rates to these various drugs. For example, they found the INH-resistant forms appeared approximately once in 100,000 normal cells, and streptomycin resistant forms once in 1,000,000 cells. The number of cells resistant to both drugs given together was only a very few, something like one in 10,000,000,000 cells. Practical means of combatting resistance have included giving drugs in adequate dosage and/or in combination of the drugs to prevent the emergence of resistant mutants.

The fact is that these forms which generally are resistant to the common antibiotics have become a big problem in the treatment of cases

from which they come and a possible public health problem if other uninfected cases are infected by them.

We know that the bacillary population of drug-treated cases is suddenly revolutionized with the typical forms being wiped out leaving behind all kinds of resistant forms, some of which are atypical.

If the proper dosage and combination of drugs is given, many virulent mutants may be prevented, but the facts remain that a great many physicians do not give proper dosage, do not give the treatment long enough and do not inquire into the patient's honesty to see if he is taking the drugs as prescribed. Furthermore, many patients leave the hospital without medical advice and cause various interruptions of treatment.

Since there are no new drugs at the present time that will supply all the needs in the treatment of tuberculosis, research should be extended in the fields of bacteriology, genetics, and biochemistry with the use of every available means to try to solve these problems. All efforts should be made to use the atomic indicators such as carbon 14, phosphorus 32, and nitrogen 15 as well as x-ray stimulation, chemical irritation, and any other available means with the ultimate aim to improve the results of treatment. The newer sciences will greatly aid us. We should especially become more chemically minded. When we consider all that has been done and is being done in various research studies in the various specialties mentioned, we can come to no other conclusion than that the key to understanding of bacterial change is in mutation. Furthermore, all biological change, including mutation, specific immunity, enzyme activity and hereditary traits are in the last analysis an expression of chemical or physio-chemical action.

In a final appraisal of the "atypical" tubercle bacilli, it is obvious that there are new facts appearing as a result of recent discoveries that should help to give a better understanding of the cause as well as better methods for handling the various problems that have arisen.

SUMMARY

Atypical forms of *M. tuberculosis* have been discussed from the earliest identification of variations to the present time, and instead of being a mystery, it is all within the laws of biology. While there may be phenomena not yet clearly understood in the life of bacteria, the mutation theory of DeVries seems to be adequate to explain most of the changes that have appeared and are continuing to appear as they do in other forms of life.

Even before the recent work, the mutation theory was plausible; where changes could be demonstrated by stimulants, such as the x-ray and chemicals on certain species of life. The biochemical and x-ray identification of the structure of giant molecules in the chromosomes are more revealing and convincing. Sometimes major displacements occur within the molecule so that the new molecule is sufficiently different to result in variation of the progeny. These changes are a continuing process throughout life on the earth and help explain the presence of the widespread of life. When there has been a radical change in the environment, a mutant may result and will grow when all the other forms, including the parent strains, are suppressed or are over-grown.

Use of antimicrobial drugs has brought the phenomenon into clear perspective. The drugs have blocked the formation of new molecules leaving the mutants free to overgrow the parents as resistant forms. The question whether drugs cause mutation is still unanswered, but the wiping out of the sensitive parent forms no doubt leaves a greater number of atypical bacilli.

Attempts are being made to classify the various atypical forms. Many of them still retain varying degrees of virulence for the human host and thereby create problems.

RESUMEN

Las formas antipicas del M. tuberculosis se han discutido desde las mas tempranas identificaciones de los variantes hasta el momento actual y en lugar de ser un misterio

estan dentro de las leyes de la biologia. Si bien puede haber fenómenos no comprendidos claramente en la vida de las bacterias, la teoría de la mutación de De Vries, parece que es adecuada para explicar la mayoría de los cambios que han aparecido y continúan haciéndolo como ocurren en otras formas de la vida.

Aún antes del trabajo reciente, la teoría de la mutación era plausible; cuando se podían demostrar cambios por los estímulos como los rayos X, las substancias químicas en ciertas especias de la vida. La identificación bioquímica y a los rayos X de la estructura de las moléculas gigantes en los cromosomas son las más reveladoras y convincentes. Algunas veces, deplazamientos grandes ocurren dentro de las moléculas, de manera que la nueva molécula es suficientemente diferente para conducir a una variación en la progenie. Estos cambios son un proceso continuo a través de la vida sobre la tierra. Cuando hay un cambio en el medio puede résultar un mutante y este crecerá cuando todas las demás formas incluyendo las cepas parientes, se suprimen o han sido sobrepasadas.

El uso del as drogas antimicrobianas ha traído el fenómeno a una perspectiva clara. Las drogas han contenido la formación de nuevas moléculas dejando a los mutantes libres para sobrecrecer a sus parientes como formas de resistencia. La cuestión de si las drogas causan la mutación, aún no está resuelta pero la desaparición de las cepas parientes sensibles, no hay duda de que deja un mayor número de gérmenes atípicos.

Se estan haciendo intentos de clasificar las formas atípicas. Muchas de ellas aún retienen grados variablse de virulencia para el ser humano y por tanto han creado problemas.

ZUSAMMENFASSUNG

Atypische Formen des M. tuberculosis wurden erörtert von der Periode der frühesten Feststellung von Variaten bis zum heutigen Tag; und weit entfernt davon, ein Mysterium zu sein, liegt das alles im Rahmen der biologischen Gesetze. Mag es Phönomene geben im Leben der Bakterien, die bisher nicht recht verständlich erscheinen, so dürfte die Mutationstheorie von DeVries geeignet sein, die meisten der aufgetretenen Veränderungen zu erklären, die noch ständig in anderen Formen des Lebens vonstatten gehen. Selbst angesichts der jüngsten Untersuchungen war die Mutationstheorie einleichtend, als Veränderungen durch Stimulantien nachgewiesen werden konnten, so wie es die Röntgenstrahlen und chemischen Stoffe auf gewisse lebendige Spezies bewirken. Die biochemische und röntgenologische Aufklärung der Struktur von Riesenmollekülen in den Chromosomen sind aufschlußreicher und überzeugender. Gelegentlich kommt es zu größeren Verschiebungen innerhalb der Moleküle, so daß Variationen in der Nachkommenschaft daraus resultieren. Diese Wandlungen sind ein fortlaufendes Geschehen alles Lebendigen auf der Erde. Sie tragen dazu bei, eine Erklärung abzugeben für das Bestehen einer Vielfalt von Leben. Kam es zu einem radikalen Wandel der Umwelt, war möglicherweise eine Mutation die Folge und vermochte zu gedeihen, während alle anderen Formen einschliesslich der ursprünglichen Stämme verdrängt oder überwuchert waren.

Der Gebrauch von antimikrobiellen Arzneimitteln hat das Phänomen klar zur Anschauung gebracht. Die Wirkstoffe haben die Bildung neuer Moleküle blockiert und ermöglichten es den Varianten als resistente Formen, die Ausgangsstämme zu überwuchern. Es ist die Frage noch unbeantwortet, ob Arzneimittel zu einer Mutation führen können, aber die Ausschaltung der sensiblen Ausgangsformen liefert ohne Zweifel eine größere Anzahl atypischer Formen.

Es sind Versuche unternommen worden, die verschiedenen atypischen Formen zu klassifizieren. Viele von ihnen behalten noch ein verschieedn starkes Maß von Virulenz für den menschlichen Wert und bedeuten daher ein Problem.

Complete reference list will appear in reprints.

DETECTION OF HEART DISEASE

The electrocardiogram, spatial vectorcardiogram, and ventricular gradient were studied in 15 patients with pre-excitation (Wolff-Parkinson-White) syndrome to determine their usefulness in the recognition of myocardial disease in the presence of this disturbance. It was found that the spatial vectorcardiogram and ventricular gradient could suggest the diagnosis of myocardial disease in patients with this syndrome. These studies further indicate the value of the spatial vectorcardiogram in clinical cardiology.

Burch, G. E., and DePasquale, N. P.: "Electrocardiographic and Vectorcardiographic Detection of Heart Disease in the Presence of the Pre-excitation Syndrome (Wolff-Parkinson-White Syndrome)," *Ann. Int. Med.*, 54:387, 1961.

Chemical Pneumonitis from Inhalation of Zinc Chloride

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For a long time, the inhalation of elemental heavy metal fumes or particulate suspensions of heavy metal salts has been associated with the production of various types of injury to the upper respiratory passages and lung parenchyma. The majority of case reports involving the inhalation of zinc compounds were published prior to 1950. The characteristic, but unusual features of three cases recently treated at the United States Air Force Hospital, Lackland, prompted this report.

Case 1: A 17 year-old airman undergoing basic training was seen at the emergency facility of this hospital early on the 13th of July, 1959, following an accidental overexposure to screening smoke during routine survival training. His complaints were "burning of the throat," paroxysmal coughing, nausea and retching. Physical examination one hour after exposure was unremarkable except for oral temperature of 99.6°F. and respiratory rate of 26 per minute. Symptoms of coughing and nausea disappeared rapidly on supportive therapy and bed rest. A repeat physical examination six hours later was entirely negative, and he was returned to duty.

During the next 48 hours, he noticed increasing dyspnea, feverishness, and malaise, and was re-admitted to the hospital. At this time, the only abnormal physical finding was an oral temperature of 102.6°F. All laboratory work was normal except for white blood count of 11,700 cells per cubic millimeter and a chest roentgenogram revealing a moderately dense, diffuse infiltrative process throughout both lung fields. The differential white blood showed a shift to the left and a 6 per cent eosinophilia.

The initial treatment regimen consisted of saturated solution of potassium iodide, tetracycline and bed rest. Although he was comfortable, with only a rare non productive cough, his temperature climbed to 105.2°F. and he developed tachypnea and definite cyanosis. A repeat posteroanterior chest x-ray film (Fig. 1) showed progression of his infiltrate, even though the physical examination of the chest was still unremarkable.

He was given intermittent positive pressure breathing with 100 per cent oxygen with little effect and finally 250 mg. of hydrocortisone was administered intravenously over the next 14 hours. The temperature dropped 2°F. during the first hour of this treatment and was normal within six hours of initiation of the course of treatment. Tachypnea decreased and his color improved concomitantly.

Positive pressure breathing was continued intermittently for the next five days and steroid administration in the form of oral prednisolone was continued for 12 days. A low grade tachypnea and sporadic temperature elevations (up to 101.0°F.) continued for the first 72 hours. After this, the patient was essentially asymptomatic.

In spite of marked earlier clinical improvement, initial clearing of the infiltrate viewed by x-ray film was not observed for 11 days, and final resolution was delayed for over one month (Fig. 2). Repeated throat and sputum cultures revealed only normal flora. The only pulmonary ventilatory abnormality was the reduced vital capacity of 75.8 per cent of the predicted normal value, which later increased to 99.6 per cent of the predicted normal value after convalescence. The patient's 24 hour zinc urinary excretion was 3.02 mg. during early convalescence (upper limits of normal 1.0 mg. per day).

Case 2: A 17 year-old basic airman was admitted to the same facility approximately one-half hour after excessive smoke exposure, complaining of cough, dyspnea, and "burning of the throat." The only abnormal physical findings were oral temperature of 101.0°F., respiratory rate of 38 per minute, and mildly injected pharyngeal mucosa. He was treated with salicylates, elixir of terpin hydrate and bed rest. Dyspnea, coughing and mild malaise disappeared within six hours, but temperature remained elevated (up to 101.6°F.) and a few rales were heard in the left lung base. A postero-

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anterior chest roentgenogram taken the following day was normal, and the patient complained only of slight tightness in the chest. Because of the persistent fever and fine rales in the left posterior chest, a posteroanterior chest x-ray film was taken the next day, which showed a faint, diffuse infiltrate in the left mid-lung field. Routine laboratory examinations were unremarkable, except for an elevated white blood count of 11,800 cells per cubic millimeter and an increase in the percentage of polymorphonuclear cells on differential count. A chest x-ray film taken five days after admission showed an increase in the patchy infiltration in the left mid-lung field with a fainter infiltration in the opposite side (Fig. 3). Radiographic resolution was virtually complete in one month, while he was essentially afebrile and asymptomatic after the fourth hospital day and had uneventful convalescense. (Fig. 4). He received only supportive therapy during his hospitalization.

He had a borderline normal vital capacity of 82 per cent of predicted normal levels, and a resting blood oxyhemoglobin saturation of 97.7 per cent at the height of his infiltrate. After recovery the vital capacity improved to the level of 95 per cent of predicted normal. The highest 24-hour zinc urinary excretion obtained in this patient was 1.74 mg.

Case 3: A 19 year-old airman was admitted to the hospital on August 5, 1959, complaining of breathlessness, nausea, cough and "tightness of the chest," shortly after a five-minute exposure to smoke fumes. Physical examination revealed only tachypnea, medium pitched expiratory ronchi and mild obesity. The temperature was normal and no cyanosis was seen. The tachypnea, nausea, and coughing diminished late that day, although the temperature rose to 102°F. in the absence of any new symptom. The initial routine laboratory results were within normal limits. A posteroanterior chest roentgenogram taken 24 hours after admission showed an infiltrative process involving the left lower lung field and lingula and mild dorsal scoliosis. A repeat chest x-ray film four days after admission showed a more generalized extension of the infiltrate (Fig. 5).

Mild malaise, dyspnea and a nonproductive cough with slight fever were present during the first 72 hours, but thereafter he was virtually asymptomatic. Treatment was limited to bed rest for 48 hours and elixir of terpin hydrate and aspirin given for the temperature elevations. Except for an occasional ronchus which was heard only early in the hospitalization, auscultation and percussion of the chest were nonrevealing. Radiographic resolution was virtually complete in 16 days (Fig. 6).

Cold agglutinins were not present. Viral agglutination studies for psittacosis, adenoviruses and the influenza group showed no diagnostic rise in titre, and throat and sputum cultures revealed only normal bacterial flora.

The only pulmonary ventilatory function abnormality noted was a vital capacity of 65.8 per cent of the predicted normal value, which improved to 87.3 per cent after recovery. At the height of the patient's clinical illness, his resting blood oxyhemoglobin saturation was 94.5 per cent.

FIGURE 1

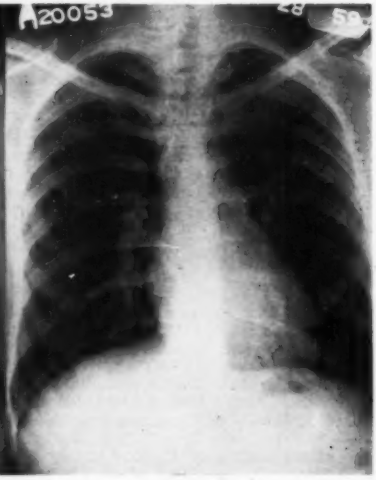

FIGURE 2

FIGURE 1 (Case 1): Extensive bilateral pneumonitis in the presence of minimal chest physical findings. FIGURE 2 (Case 1): Resolution of pneumonitis six weeks after smoke inhalation.

TABLE 1—TOXICOLOGIC ANALYSIS OF AIR SAMPLE COLLECTED AT SCENE OF EXPOSURE*

Material	Concentration
Total particulate matter:	800.0 mg./cu. meter
Aluminum chloride	334.2 mg./cu. meter
Aluminum oxide	134.6 mg./cu. meter
Zinc chloride	4075.0 mg./cu. meter
Zinc oxide	107.6 mg./cu. meter

(Particle size ranged from 0..01 micron to 25 microns. Average size was 0.1 micron.)

*Reaction products of combustion of zinc oxide, grained aluminum and hexochloroethane grenade.

Discussion

Chemical injury to the respiratory tract and lung parenchyma from a variety of vaporized elemental metal fumes or finely divided suspensions of metal salts has been reported and discussed, particularly in the industrial literature. Intoxication to zinc compounds has been reported primarily as a syndrome of "metal fume fever,"[1-5] developing after the inhalation of suspensions of finely divided zinc oxide. Reports of intoxication to zinc chloride, however, have been sparse and usually related to accidental overexposure of military personnel to smoke screening materials.[6,7]

A smoke screening compound containing white phosphorous, titanium tetrachloride, and petroleum-steam produces predominantly zinc chloride and aluminum oxide after ignition. The average particle size under our test conditions was 0.1 micron (Table 1). In general, zinc chloride in extremely high concentration of finely divided particles will produce a chemical irritation of the upper respiratory tract. However, in concentrations usually encountered, zinc chloride more typically inflicts an insidious interstitial pneumonitis because of the small size of its particles and its relatively low solubility.

Pathologic changes following inhalation of zinc chloride have been described by Evans,[6] who analyzed casualties following severe overexposure of screening smoke at Malta in 1945. Of 70 people exposed, 17 required hospitalization and 10 died. The two autopsies which were performed showed injection, congestion, ulceration, and necrosis of the upper respiratory tract with patchy pneumonitis, localized emphysema and subpleural hemorrhage. Most survivors were improved after ten days. Later examination of the survivors suggested complete recovery.

In contrast to this report, our patients experienced only moderate overexposure to zinc chloride. In all three of them, the initial symptoms such as nausea, paroxysmal cough, dyspnea and tightness of the chest, disappeared after six hours of conservative care. However, fever, tachypnea and cyanosis later developed and were particularly noticeable in the first patient. Later in the course of the illness, coughing was nonproductive and infrequent despite the presence of marked parenchymal infiltration

FIGURE 3 FIGURE 4

FIGURE 3 (Case 2): Diffuse pneumonitis one week after smoke inhalation.
FIGURE 4 (Case 2): Resolution of pneumonitis approximately one month after exposure.

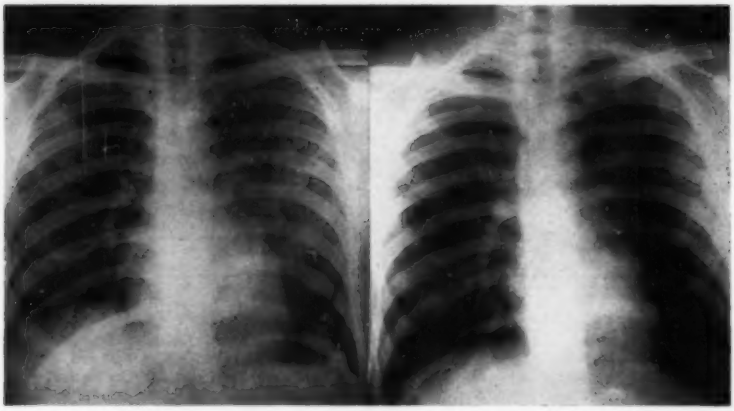

FIGURE 5 FIGURE 6

FIGURE 5 (Case 3): Bilateral pneumonitis five days after smoke inhalation.
FIGURE 6 (Case 3): Final resolution of pneumonia.

on the roentgenograms. Auscultation of the lungs revealed only occasional ronchi and a few medium rales in one patient despite the density of the pneumonitis suggested by x-ray film. As in other reports, the depressed vital capacity during the acute illness reverted to normal in all patients.

The absence of prolonged leukocytes, productive cough or typical septic course in all three patients was interpreted as evidence against bacterial pneumonitis. Cultures of the throat, sputum and blood were negative for pathogens. In one ptaient, the absence of cold agglutinins and significant titres of respiratory virus agglutinations were taken as evidence against the presence of a viral pneumonitis. In two patients, initial 24-hour zinc urinary excretions, as measured by the method of Snell and Snell,[8] were larger than those found later in the disease. While zinc excretion can vary widely, depending on the diet, they were above the upper limits of normal values established by Drinker,[9] and would tend to indicate that an excretion of inhaled zinc occurred.

Treatment

From a review of the literature on the treatment of respiratory tract and pulmonary injuries following inhalation of irritating substances, the outstanding principle of treatment is that of *watchful expectancy*. The rapidity and the magnitude of pneumonitic involvement in patients whose earliest complaints and physical examination suggested minimal pathology were striking.

Classically the use of bronchodilators, oxygen by mask, tent or positive pressure, has been recommended in the older literature.[10-11] In addition, venesection has been recommended to relieve acute pulmonary edema. The use of ACTH or corticosteroids has been of dramatic, lifesaving importance in the management of subacute and chronic pulmonary inflammation following inhalation injury.[12] The use of antibiotics in treating secondary infection is legion, but prophylactic administration is recommended by several authors.[13,14] Most recently chelating agents have been suggested as a rationale, and perhaps lifesaving, treatment for pulmonary infiltrations caused by heavy metals.[15] In the treatment of our severely ill patient, chelating agents were considered but not used inasmuch as the response to steroid administration was so prompt and efficacious.

SUMMARY

Three cases of severe, generalized chemical pneumonitis resulting from exposure to zinc chloride have been presented with representative roentgenograms. Two responded to symptomatic treatment while under close observation and one showed rapid progression and demanded the most aggressive measures. Despite the generalized involvement in all three patients and the relatively long persistence of infiltrate on chest roentgenograms, no lasting effects were detected by analysis of follow-up symptoms, chest x-ray films, ventilatory function tests or blood gas studies.

From a modest review of the literature, it is believed that the use of adrenocortical steroids during the acute phase of chemical pneumonitis has not been properly emphasized. Since the earliest complaints or findings are notoriously minimal, we wish to re-emphasize the cardinal principle of the closest watchful expectancy in patients recently exposed to noxious inhalant vapors.

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RESUMEN

Se han presentado tres casos de neumonitis grave generalizada que resultó de exposición a cloruro de zinc, mostrando los cuadros radiológicos representativos.

Dos respondieron al tratamiento sintomático bajo una observación cuidadosa y uno mostró rápido empeoramiento y requirió las medidas más enérgicas. A pesar de la afección generalizada en los tres enfermos y de la persistencia relativamente larga de la infiltración, según los roentgenogramas, no quedaron efectos duraderos que se pudieran descubrir por la observación, los rayos X, la función ventilatoria o las estudios de los gases en la sangre.

De una modesta revisión de la literatura, se desprende y así se cree que el uso de los adrenocorticoides durante la fase aguda de la neumonitis química no ha sido bien enfatizada. Puesto que las molestias al principio o los hallazgos son notablemente mínimos, queremos recalcar el principio cardinal de la vigilancia mas testrecha en los enfermos expuestos a vapores inhalados dañinos.

RESUMÉ

Les auteurs présentent trois cas the pneumonie chimique grave généralisée, résultant d'une exposition au chlorure de zinc aver radiographies caractéristiques. Deux d'ntre eu ont réagi au traitment symptomatique observation minutieuse, et le troisième une évolution très rapide at a nécessité les mesures les plus énergiques. En dépit de la généralisation de l'atteinte chez ces trois malades, et de la persistance relativement longue des infiltrats sur les radiographies pulmonaires, auucune séquelle à longue échéance n'a pu être détectée par l'analyse des symptôms ultérieurs, l'étude radiologique, les examens functionnels, et l'étude des gas du sang.

En faisant une revue modeste de la littérature, les auteurs pensent que l'utilisation de stéroïdes adréno-corticaux pendant la phase aiguë de pneumonie chimique n'a pas été suffisamment mise en valeur. Puisque les toutes premières manifestations très discrets, les auteurs veuulent insister de nouveau sur le principe fondamental qui est la surveillance vigilante de tout malade récemment exposé à des vapeurs toxiques.

ZUSAMMENFASSUNG

Bericht über drei Fälle von schwerer generalisierter chemischer Pneumonitis mit typischen Röntgenaufnahmen als Folge einer Exposition mit Zinkchlorid. 2 Fälle reagierten auf eine symptomatische Behandlung bei sehr genauer Beobachtung, und 1 Fall zeigte eine rasche Progredienz und erforderte besonders eingreifende Maßnahmen. Trotz der Mitbeteiligung des Gesamtorganismus bei allen drei Kranken und des relativ langen Anhaltens der Infiltrate auf den Thoraxröntgenaufnahmen ließen sich keine Dauerfolgen nachweisen an Hand der Auswertung der Symptome, der Thoraxröntgenaufnahmen, der Lungenleistungsproben und Blutgasanalysen währen der Nachbeobachtung.

An Hand einer kurzen Literaturübersicht wird die Auffassung vertreten, daß die Verwendung von Nebennierenrinden-Steroiden während der akuten Phase einer chemischen Pneumonitis nicht genau herausgehoben worden ist. Da die allerersten Beschwerde oder Befunde offenkundig minimal sind, möchten wir neuerlich das Kardinalprinzip des sorgfältigst beobachtenden Abwartens betonen bei Patienten, die kurz zuvor die Atemwege schädigenden Dämpfen ausgesetzt gewesen waren.

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SECONDARY PRIMARY BRONCHOGENIC CARCINOMA

In following the postoperative course of 63 thirty-month survivors of lung cancer surgery, four cases (6.4 per cent) of second primary bronchogenic carcinoma were discovered. An evaluation of the clinical histories and pathologic findings, together with pertinent facts on patient survival after pulmonary cancer surgery, provides acceptable reasons for considering these patients as having second primary lung cancers. Three of the patients, all having undergone pneumonectomy as initial therapy, died of respiratory failure shortly after the discovery of the second pulmonary malignancy. In these patients, the second cancer was discovered during the 52nd, 64th and 71st postoperative month of survival. They represent 20 per cent of the 15 survivors who died during the third, fourth and fifth years of survival. One patient who had a lobectomy as the initial procedure and who developed a second contralateral primary lesion after 33 months, is alive and free of disease 32 months after a second lobectomy.

This study provides ample justification for careful and repeated follow-up examinations for all patients surviving lung cancer surgery in excess of 30 months. The successful outcome of the patient who survived two primary cancers, each treated by lobectomy, suggests that lobectomy is to be preferred over pneumonectomy in those cases in which the choice between the two exists without impairing the changes for initial cure.

In view of the apparent parallel with oral cavity cancer and in recognition of the association of carcinoma-in-situ and invasive carcinoma in widely separated regions of the respiratory tree, the development of second primary carcinomas of the lung should come as no surprise and could have been anticipated. Any highly successful therapy for lung cancer may not only have to obliterate the manifest cancer, but also will have to deal in some way with a respiratory mucosa that is cancer prone.

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Lung Abscess as Seen in a Municipal Hospital

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Introduction

The observation that the typical picture and prognosis of lung abscesses in a municipal hospital appeared to be different from the classical description[1-4] prompted the present investigation. Further evaluation of this disease may help to improve diagnosis and treatment so that results in a general hospital approximate those obtained in reported series of "primary" lung abscess.[5-8]

Materials and Methods

All lung abscesses, a total of 95 cases, diagnosed at the Milwaukee County General Hospital from January, 1950, through December, 1958, were reviewed. The incidence remained constant during these years. Excluded were cases of minute embolic lung abscesses, bronchiectasis, tuberculous cavities, infected congenital cysts, hydatid cysts, and abscesses due to central necrosis of extensive neoplasms.

The following data were recorded in each case: age, race, sex, length of hospitalization, relationship between time of diagnosis and prognosis, associated diseases, methods of diagnosis, presenting symptoms, findings on physical examination, laboratory studies, results of therapy, and radiologic findings. Differences between the fatal and non-fatal groups were determined.

Results

The ages ranged from less than one year to 89 years. The highest incidence was in the eighth decade where 23 of the 95 cases occurred. There were 74 males and 21 females. Eighty-four patients were white and 11 were Negroes which is an approximation of the ratio of the races admitted to the hospital during the period of study (Table 1). The gross mortality was 61 of 95 patients (63 per cent). It should be pointed out, however, that many of these patients died from underlying diseases. Old age was not the most important factor in mortality since 11 of the 16 patients under the age of 40 also died. In this relatively young group, however, the associated diseases may have been the decisive factor in mortality. These included severe preceding respiratory diseases such as empyema with bronchopleural fistula, tracheoesophageal fistula, pulmonary infarction, extensive pneumonia, carcinoma, and cardiovascular disease. In addition, two patients had glomerulonephritis, two had bacterial endocarditis, one was a diabetic alcoholic, and one had developed his lung abscess while in a respirator because of bulbar poliomyelitis.

Analysis of the correlation between the time of diagnosis and mortality revealed that of the 34 non-fatal cases, 17 were diagnosed within

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the first week. Thus, as might be expected, the cases in which diagnosis was made shortly after admission appeared to have a better prognosis.

The time interval between the onset of symptoms and the establishment of a definite diagnosis was not significantly different in the fatal and non-fatal group. The mean value for the fatal and non-fatal group were 60 and 61 days respectively. Explanations for this delay in diagnosis, in retrospect, are that lung abscess may have an insidious onset, overshadowed by concomitant disease or that symptoms may have existed for some time before medical help was sought.

Forty-five of the 61 fatal cases had necropsies. In 38 of these (84 per cent) the existence of the lung abscess was not realized until discovery at the postmortem examination. This finding would lead one to suspect that unrecognized terminal lung abscesses occur rather frequently.

An attempt was made to determine the place of onset in each case and all indications were that 37 of the 95 patients developed lung abscess during their hospitalization. These 37 patients were not found to differ significantly from the group as a whole. As shown in Table 2, aspiration seems to be the most common contributory factor in the establishment of these abscesses.

Diagnosis was made antemortem in 57 cases. In 54 of these it was first made by roentgenologic examination, in one case by thoracotomy and in only two was the diagnosis first suspected by physical examination. The reasons 38 of the cases were not diagnosed during life may be that the severity of the underlying disease often resulted in lack of x-ray studies and that preceding treatment with antibiotics may have camouflaged the serious pulmonary process.

The clinical picture of lung abscess has been described as that of a febrile illness of rather sudden onset, usually preceded by episodes of unconsciousness, general anesthesia, cerebral vascular accidents, or cranio-cerebral trauma. Copious foul sputum is often mentioned.[1-4]

The clinical picture presented by the 95 patients in this report differed considerably and was one of insidious onset of a symptom complex which included cough, purulent sputum (rarely malodorous), chest pain, and hemoptysis. Cough was the most prominent symptom and was recorded in 71 patients. Purulent sputum was next in frequency and noted

TABLE 1 — AGE, SEX, RACE, AND MORTALITY IN CASES OF LUNG ABSCESS IN A MUNICIPAL HOSPITAL

Race	Sex	Age in Years 1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Over 81	Total
White	Male	1		2	2	1	7	12	14	5	44
White	Female			1	1	1	2	1	5	2	13
Negro	Male		2	1	1						4
Negro	Female	1		1		1	1				4
Total		1	2	4	4	2	9	13	19	7	61

Cases above the dotted lines survived. Cases below the dotted lines died.

TABLE 2 — FACTORS PROBABLY RESPONSIBLE FOR THE DEVELOPMENT OF LUNG ABSCESS DURING HOSPITALIZATION

Factor	Died	Recovered	Died	Recovered
Aspiration associated with:				
a. Operative or immediate postoperative period	4	3		
b. Stupor or coma	5			
c. Repeated vomiting	4			
d. Convulsive therapy		1		
f. Tracheotomy		1		
Total			15	3
Preceding pulmonary disease			6	6
Septicemia			5	
Pulmonary embolism			2	
Total			28	9

in 55 patients, 24 with copious amounts. The history of chest pain was elicited in 48 patients, hemoptysis in 26 and vomiting, that may have resulted in aspiration, in 22. "Foul sputum" occurred in only nine cases.

The recorded physical findings showed 52 patients to have rales and 30 dullness to percussion.

Previous infections were noted and as a group, the patients did not appear to be subject to frequent infections although 14 of them had a history of pneumonia in the past.

The composite laboratory findings were those of a mild anemia (mean hemoglobin level 11.3 gm. per cent), a significant leukocytosis (mean white blood count 18,000) without as great a percentage of polymorphonuclear leukocytes as might be expected in the presence of abscess (mean percentage of polymorphonuclear leukocytes 45 per cent), an elevated sedimentation rate (80 mm. per hour [Westergren]), and not infrequently albuminuria.

An analysis of differences in laboratory findings revealed significantly higher sedimentation rates among the survivors and significantly greater percentages of "band forms" of polymorphonuclear leukocytes and more abnormal urinalyses in the fatal group. The mean sedimentation rates of those surviving was 96 mm. per hour as contrasted to a rate of 70 mm. per hour among the fatalities.

The results of bacterial cultures of sputum or bronchial washings were available on 54 patients (Table 3). The most commonly isolated organ-

TABLE 3 — BACTERIOLOGIC FINDINGS IN LUNG ABSCESS

Bacteria	Non-fatal	Fatal	Total
Staphylococcus aureus	12	11	23
Staphylococcus albus	6	6	12
Beta hemolytic streptococci	2	2	4
Escherichia coli	6	5	11
Pseudomonas aeruginosa	3	3	6
Candida albicans	—	2	2
Friedländer's bacillus	—	1	1
Proteus	—	2	2
Pneumococcus	—	1	1
Geotrichum	1	—	1
Neisseria catarrhalis			
Streptococcus viridans			
B. subtilis	11	7	18

ism was the Staphylococcus with a variety of other bacteria being found in addtion. The patients who died did not have significantly different bacteriologic findings than did those who survived. The widespread distribution of all the species of bacteria cultured made it impossible to be sure of their role in the pathogenesis of the abscesses from which they were cultured.

Evaluation of therapy was particularly difficult due to the many therapeutic regimens used during the course of this study. It was decided to see how many patients survived who were treated with each of the specific agents used even though this method of evaluation is open to some criticism due to the fact that many of the patients died mainly of associated diseases. The results of therapy with the various antibiotics are presented in Table 4. This table may be interpreted as showing that all of the antibiotics used may have been helpful in certain cases and that patients who received more than one agent usually did better, since only five of 28 patients treated with a single agent survived. Table 4 also shows an analysis of therapeutic effectiveness of agents that were used by design or good fortune in cases in which specific bacteria cultured from the sputum were sensitive *in vitro* to them. The value of specific therapy with combinations of antibiotics selected on the basis of *in vitro* sensitivity tests seems apparent.

Twenty-nine of the 95 patients had operative procedures. Fifteen of these had various thoracic operations as treatment of their lung abscesses and 14 had surgical procedures prior to the development of their lung abscesses. Of this latter group, only four had thoracic operations. In the group of 15 operated on for lung abscess, four died, but this mortality can perhaps be rationalized by the age of the patients and/or serious associated diseases.

All the available chest x-ray films of the patients were reviewed in order to determine the sites most commonly involved and the difference in size of the abscess in fatal and non-fatal cases. Films of 51 of the 95 patients were available. In 20 the abscesses were located in the right mid and lower zones. In seven they were found in the left lower zone

TABLE 4 — COMPARISON OF RESULTS OF THERAPY GIVEN EMPIRICALLY AND AFTER RESULTS OF *IN VITRO* SENSITIVITY TESTS

	Therapy Without Regard for Sensitivity Test			Therapy When Isolated Bacteria Was Sensitive to Agent Used		
Drug	No. of Pts.	Recovered	Died	No. of Times Used	Recovered	Died
Penicillin	60	33	27	24	15	9
Streptomycin	24	9	15	5	4	1
Oxytetracycline	11	5	6	2	2	—
Chloramphenicol	30	17	13	8	7	1
Erythromycin	13	9	4	3	3	—
Neomycin	16	11	5	9	8	1
Chlortetracycline	13	6	7	2	2	—
Aerosol Neomycin*	23	14	9			
Vancomycin	2	2	1			
Combined antibiotics	34	17	17			
Antibiotics in succession	20	9	11			
Single antibiotics	23	5	18			
Total	269	136	133	53	41	12

*Waisbren, B. A.: "Neomycin," *Practitioner*, 176:39-46, 1956.

and in seven in the left upper zone. Right upper zone abscesses were found in only five cases. Bilateral abscesses in both lower zones were seen in three cases and the remainder were found in other distributions. Comparisons between the fatal and non-fatal cases shows that the abscesses were located in the right mid zone in six fatal and four non-fatal cases, and in the right lower zone in four fatal and six non-fatal cases. Therefore, in the cases available, there did not seem to be much correlation between the location of the abscess and the outcome. The largest diameter in each lung abscess was measured and recorded. An attempt was made to correlate this finding with the prognosis. The largest abscess diameter found was 14 cm. and this occurred in a fatal case. The average diameters were calculated in both groups and turned out to be exactly the same, namely 6.2 cm. for the fatal as well as for the non-fatal group. The majority of the lung abscesses (61 per cent) showed fluid levels at some stage of their development.

Discussion

The important feature of this study is the demonstration of the difference between all the unselected lung abscesses in a general hospital and the reported series of primary pulmonary abscesses.[5-6] The analyzed 95 cases are all of the cases of lung abscess on record regardless of whether this entity was the primary disease, an associated illness, or even only an unexpected finding at necropsy. The reports in the literature, however, consist usually of selected cases of uncomplicated lung abscess and this contrast is reflected in a comparison of the mortality rates. In this series the mortality is even higher than that recorded prior to the antibiotic era in which Allen and Blackman[9] calculated in 1936 from 2,114 cases of lung abscesses a surgical mortality of 34.4 per cent and a combined medical and surgical mortality of 32.2 per cent. An analysis of 100 cases of their own showed a total mortality of 34 per cent. A report by Sweet[10] in 1945 of the cases of lung abscess at Massachusetts General Hospital from 1938 through 1942 revealed in 120 cases a medical mortality of 24.4 per cent and a surgical mortality of 14.5 per cent. These results, outstanding for that period, were attributed to sulphonamides and team work. A higher mortality was reported by Smith[11] in 1948 who showed a mortality of 34.7 per cent in cases treated medically and 32.7 per cent for the surgical cases in the period from 1940 to 1945. The picture improved subsequently with the advent of penicillin and other antibiotics. This change is described in a number of reports.[12-17] Wolcott and Murphy[18] gave a fatality of 31.5 per cent for the years 1941 to 1944, then 17.2 per cent for the years 1945 until 1951, and 0 per cent for the period of 1953 to 1955. A more recent series,[19] however, of 70 cases of pulmonary abscess, contrasts significantly in the following points: only 5.7 per cent of the patients were older than 60 years, the lung abscess was the predominant disease entity, and, despite a combined medical and surgical team, the mortality remained as high as 17.1 per cent. A certain vacillation from pure medical management prior to the introduction of open drainage by Neuhoff and Touroff[20] to the consideration of lung abscess as an absolute surgical indication[21-25] also reflects the changing attitude toward the disease. In recent years, the pendulum has swung back and a number of reports indicate that lung abscess should be considered primarily a medical problem.[5,19,26,27,28,29] The present series, of course, offers no decision in this respect since the vast majority of patients were medical and the surgical series is too small.

It is apparent that lung abscess as reported in this study is a different entity from the carefully selected patients reported in other series. In none of the series reviewed were cases included in whom the abscesses were diagnosed only at necropsy as occurred in 38 of these 95 cases. However, even if the cases found at necropsy were not included, the mortality of 23 out of 57 cases (40.3 per cent) is definitely higher than that reported by other authors. This is in spite of the fact that most of these patients were treated with chemotherapy and some by surgical means. The main reason for differences between this report and other publications is that no attempt has been made to select uncomplicated cases and this included all cases of lung abscesses that were recorded and coded during the period studied. Therefore, many of the patients died from complications of their other illnesses and the lung abscess could not be considered the sole cause of demise. The authors are aware that the use of all inclusive data of this sort in regard to a disease entity is not applicable to comparative studies, but is thought to be particularly valuable as a base line for comparison of incidence and treatment of this disease in their own institutions.

Only 32 bronchoscopies were done in this series and as has been emphasized by others,[7,8,30] greater use of this procedure may increase the over-all survival. This is

indicated by the fact that treatment is most effective when based on bacteriologic studies from bronchial secretions uncontaminated by oral flora. The present policy is to do bronchoscopies at the first suspicion of a lung abscess not only to obtain material for culture, but also for cytologic studies and relief of obstruction.

SUMMARY AND CONCLUSIONS

1. An analysis of 95 cases of lung abscess observed in a large municipal hospital revealed the disease to be one of insidious onset of a symptom complex which included cough, purulent sputum, chest pain, and hemoptysis that often occurs in a hospitalized patient who is suffering from another disease.

2. Sixty-one of the 95 patients died due either to the lung abscess or associated disease.

3. The best therapeutic results were obtained with multiple antibiotics selected on the basis of the *in vitro* sensitivity of pathogenic bacteria isolated from the sputum.

4. It is thought that better therapeutic results might be obtained by a higher index of suspicion regarding his disease, more vigorous attempts at isolation of the causative bacteria by bronchoscopy, and treatment by a combined medical-surgical team with multiple antibiotics selected on the basis of specific sensitivity tests.

RESUMEN

1. El análisis de 95 casos de abscesos del pulmón que se observaron en un gran hospital general, reveló que la enfermedad es de principio insidioso con un complejo sintomático que incluye tos, esputo purulento, dolor torácico, y hemoptisis y a menudo ocurre en enfermos hospitalizados que padecen de otra enfermedad.

2. De los 95 enfermos, sesenta y uno murieron ya sea del absceso o de una enferme dad asociada.

3. Los mejores resultados terapéuticos se obtienen con antibióticos múltiples escogidos sobre la base de la sensibilidad in vitro, de los gérmenes aislados del esputo.

4. Se piensa que los mejores resultados podrían obtenerse si se exaltara la sospecha de esta enfermedad y se hiciesen mayores esfuerzos para aislar las bacterias responsables por broncoscopía y si se tratan combinando medicina y cirugía en grupo que use los antibióticos múltiples escogidos de acuerdo con la sensibilidad.

ZUSAMMENFASSUNG

1. Eine Analyse von 95 Fällen von Lungenabszess, die in einem großen städtischen Krankenhaus zur Beobachtung kamen, ergab, daß diese Kranheit mit einem trügerischen Einsatz eines Symptomenkomplexes beginnt, zu dem Husten, eitriges Sputum, Brustschmerzen und Hämoptysen gehören, wie sie oft bei im Krankenhaus befindlichen Patienten auftreten, die an einer anderen Erkrankung leiden.

2. 61 von 95 Kranken starben entweder infolge ihres Lungenabszesses oder einer daran angeschlossenen Krankheit.

3. Die besten therapeutischen Resultate wurden erzielt mit Breitband-Antibiotika, die ausgewählt worden waren aufgrund von *in vitro* Sensibilitätsprüfungen von pathogenen Keimen, die ous dem Sputum isoliert waren.

4. Es wird die Auffassung vertreten, daß sich bessere therapeutische Resultate erzielen lassen, wenn der Verdacht auf eine solche Krankheit öfters ausgesprochen würde, wenn durch eine bronchoskopische tatkräftigere Untersuchung zur Isolierung der ursächlichen Bakterien an Analyse erfolgte und schliesslich durch eine Behandlung von seiten eines kombinierten internistischen und chirurgischen team's mit Breitband-Antibiotika vorgegangen würde, ausgewählt auf der Basis spezieller Sensibilitätsprüfungen.

Complete reference list will appear in reprints.

DIGITALIS AND INTESTINAL NECROSIS

Gazes and his associates describe 11 cases with acute hemorrhage and necrosis of the bowel. In all cases there was high dosage of digitalis and definite toxicity in seven. Digitalis was considered the main associated factor, especially since there was no mesenteric arterial involvement and, in four cases, there was no congestive failure at necropsy. Hepatic vein or sinusoidal sphincter constriction with resulting protal splanchnic venous congestion were considered as possible mechanisms by which digitalization produced this syndrome.

Gazes, P. C., Holmes, C. R., Moseley, V., and Pratt-Thomas, H. R.: "Acute Hemorrhage and Necrosis of the Intestines Associated with Digitalization," *Circulation*, 23:358, 1961.

A Program for Rehabilitation of Patients with Tuberculosis*,**

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Introduction

The combined program of chemotherapy with potent antimicrobial agents and decreased application of bed rest provided broad opportunities to expand rehabilitation services and to assist hospitalized tuberculous patients in all areas of social, emotional, and vocational adjustment.[1,2] Thus, at National Jewish Hospital, it became possible to offer a variety of rehabilitation services specifically designed to meet the special needs of each patient during hospitalization. Compared to the limited opportunities available under the older system of prolonged bed rest and lengthy hospitalization,[3] this was a distinct improvement.

A widely accepted contemporary philosophy of rehabilitation recognizes that many dynamic factors (physical, emotional and social), constantly interacting and dependent upon each other, must be considered in the management of hospitalized human beings. Evidently every facet of the patient's life requires consideration in determining the appropriate services needed by the individual at any given time.[4] Therefore, a closely integrated medical-rehabilitation program was developed. Patients were provided with the maximum opportunity to participate in and benefit from complete rehabilitation treatment during hospitalization.

Frequently, in reality, rehabilitation was initiated on the day the patient entered the hospital. Sometimes this occurred through formal contacts by social service and occupational therapy workers, but often on an informal basis by other individuals, including other patients. Provision was made to enable patients to remain in the hospital until all rehabilitation training had been completed. Approved medical discharge was considered only after maximum benefits had been achieved through both medical and rehabilitation treatment. In this way, the goal of having the patient leave the hospital and immediately return to community living and employment was established early during hospitalization.

Combined Organization

The specialized services of the social worker, clinical psychologist, vocational counselor, occupational therapist, and psychiatrist are required to meet the personal needs of hospitalized patients. With these specialists operating as a team, it is possible to offer rehabilitation services designed to meet the many and varied needs of such patients. Administratively, all of these services have been combined into a single operating unit, the Department of Rehabilitation Services. These services are housed in

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the National Rehabilitation Center building. The chief of each of the services is responsible to the director of the department, who in turn is directly responsible to the director of medicine. In essence, this plan is in line with the ideas of Rusk and Haas[4] who pointed out, "The inclusion of all required services under one roof and under a unified administrative structure insures the maximum utilization and most efficient operation of such a program."

While many factors influence the establishment and maintenance of an effective rehabilitation program, our experience indicates that total staff support is essential. Adequate equipment and buildings are important, but a program's success is dependent upon staff attitude. A firm conviction that rehabilitation is of great importance to each individual patient is held by all members of the Division of Medicine as well as the Department of Rehabilitation Services. These concepts have been incorporated into every phase of treatment and seem to reinforce the patient's feelings of self respect and tend to foster a positive attitude toward both hospital and treatment. In this way the setting offers every opportunity to increase the patient's acceptance, motivation and participation in medical treatment and rehabilitation.

Patient Education

The education of hospitalized patients is an important factor in reducing initial anxieties and fears concerning illness and hospitalization as well as in helping patients gain a better understanding of their illness and treatment. All newly admitted patients are encouraged to attend a series of small informal "question and answer" classroom sessions which are conducted by the medical director. The director of rehabilitation services also attends these meetings. Patients are encouraged to ask for information relevant to their illness, hospitalization, treatment, and the future. Such questions are considered in a frank and relaxed manner in order to promote better understanding of the disease tuberculosis and what the patient can expect during hospitalization. These measures are aimed at improving patient knowledge, understanding, and communication early in hospitalization, and help to promote a sense of security during this critical period of adjustment. In many instances, replacing fiction with fact tends to eliminate fears which patients harbor when they enter the hospital. The reactions and feelings of patients noted during patient education sessions also provide important clues in determining which patients might need further assistance on an individual, personal basis.

In addition, providing patients with the opportunity to meet the medical and rehabilitation directors probably reinforces the understanding that the staff, at all levels of operation, consider the patient to be more important. This plan also helps to establish a positive relationship between the staff and the patients. Thereafter, the patient has unlimited access to any member of the professional staff. The medical director reserves specific hours for patient appointments so that any one who desires may have an audience with him.

General considerations: Many of the rules and regulations governing the conduct of patients in tuberculosis hospitals seem to ignore the

rights of the individual and degrade the dignity of the person. Probably these were established without adequate knowledge. We have made a concerted effort to examine every policy affecting the management of our patients. As a result, some of the protective techniques which have been part of the treatment of tuberculosis for so many years have been eliminated or modified.

The use of masks and gowns is limited to special situations. In general, neither staff nor patients wear masks and gowns, except when the patient has a large number of tubercle bacilli in the sputum and his personal hygiene is known to be poor.[4] This program has been carried out satisfactorily for patients, staff, and community by developing and maintaining the patient's interest and motivation in practicing good habits of personal hygiene.

Some of the policies governing segregation of patients in tuberculosis hospitals tend to defeat the goal of rehabilitation by fostering excessive dependency and creating many unnecessary fears. It is important, therefore, to provide patients with the opportunity to participate in "normal life experiences" during hospitalization. As a result, all hospital activities have been opened to both male and female patients. Male and female patients eat in the same dining room, participate in the same recreational activities (including dances) and attend religious services together.

Because early physical activity is prescribed shortly after hospitalization, the majority of patients are permitted to participate in off-the-ward programs. This is modified, of course, when acute illness exists.

Patients are encouraged to participate in community activities outside the hospital as soon as their disease becomes non-infectious. For example, passes to leave the hospital are granted when the patient is able to accept responsibility for his personal hygiene and behavior. No patient who is considered sputum positive or who constitutes a hazard to the community is eligible for such passes. In this way, many of our patients are able to gain valuable experience and a sense of security about community living before discharge from the hospital.

Patients' Council

The council was developed to provide the patient population with a greater degree of participation in hospital recreation programs. Membership is open to all patients. The council is a self-governing body. Its officers are elected by a vote of all the patients on the tuberculosis service. Through the council, the patients plan their own recreational program both within the hospital and in the community.

The council also provides the staff with important information concerning the patients' concepts of the hospital program. In this way, the staff obtains information which is helpful in improving services to patients.

Training Programs

The following material identifies four theoretical programs designed to meet the varied needs of tuberculous patients. Such groupings were designed merely for simplicity of presentation. In reality, various combinations and modifications of these four programs are utilized daily.

1. *Physical Therapy Program:* This program aids in the physical restoration of the patient. Activities include exercises and tasks designed to provide improvement in coordination, balance, joint mobility, muscle strength, circulation and breathing. Both surgical and non-surgical patients make use of this program.

2. *Maintenance Program:* This program was designed to meet the needs of those patients who adjusted adequately prior to hospitalization, and have the physical and emotional capacity to return to their prehospital status after discharge. In these cases the rehabilitation goal is directed toward helping the patient maintain his level of interest and motivation through physical hardening, occupational therapy, social and leisure activities. Vocational training is used to brush up on existing skills. However, this group usually requires only minimal assistance since these individuals have many personal resources. In some instances a member of this group is motivated to obtain further vocational training in order to raise employment status and earning potential.

3. *Retraining Program:* This program is oriented primarily for those patients who, due to physical or emotional disabilities, are unable to return to former occupations or activities. Such patients need to be fully trained so they might return home and engage in gainful employment and social functioning. A complete and intensive program involving all of the rehabilitation services often is necessary for these patients.

4. *New Training Program:* This group consists of those patients who never learned a suitable occupation. Frequently, these patients have been hospitalized for long periods and/or at an age before their occupational and social abilities had been developed. As above, a total program is required, and frequently this is of long duration.

Program Co-ordination

During rehabilitation conferences, in which all the staff participate, varied understandings of the patient by the medical, nursing, and rehabilitation staffs are combined together into a total picture of the patient. Close integration of the medical and rehabilitation services, not only during such formal conferences, but at other times, make it possible to plan a comprehensive medical-rehabilitation program for each patient. Insofar as possible, every facet of the patient's social and emotional adjustment is taken into consideration in this "total" rehabilitation program.

Rehabilitation also necessitates knowledge and understanding of the family and community. Since our patients come from all parts of the country, the family that is in need of professional assistance is referred to local social or welfare agencies. In this way, assistance is made available to the family before, during, and after the patient's hospitalization.

Specialized Services

A series of prevocational, vocational and educational programs are available as part of the hospital rehabilitation program. The prevocational evaluation program is useful in providing pertinent clues and information concerning the patient's employment potential.

A prevocational assessment based upon patients' participation and performance in a variety of occupational therapy activities is made by the Occupational Therapy Service. This is an integral part of total occupational therapy services which include both physical hardening and leisure time activities.

The social worker provides important information concerning the patient's background and the unique way in which he is getting along with himself and relating to other people. Case-work treatment (psychiatrically oriented) is provided when patients encounter difficulty with respect to family matters, hospitalization and treatment. Such casework treatment on both a limited and intensive basis is available at all times.

A variety of prevocational training workshops including barbering, cosmetology, typing, bookkeeping, accounting, sewing, radio and television repair, and printing, as well as academic courses, such as English, "English for New Americans," history, and correspondence courses in several subjects are available. All of these programs are conducted by classroom teachers who are members of the hospital rehabilitation staff.

Knowledge of the patient's performance in prevocational activities is combined with information obtained from vocational and clinical psychologic testing and the reports of other members of the medical and rehabilitation staff. Periodically, the occupational therapists and the prevocational teachers complete written evaluations of each patient's progress. In this way, patients are thoroughly evaluated and arrangements made to start specific training without delay even while undergoing intensive chemotherapy. At the same time, the patient has the opportunity to test out his capacities and abilities in a variety of practical, working, prevocational situations.

When the patient is no longer considered a public hazard by the medical staff, every effort is made to continue training in an accredited community vocational program. Therefore, non-productive waste of time is reduced to a minimum.

The hospital established a special rehabilitation dormitory to make the attainment of this goal possible. This dormitory houses all patients who are no longer in need of intensive medical care and are in rehabilitation programs. Patients are provided quarters in this building until they complete rehabilitation training and are discharged from the hospital.

In order to carry out this program, close liaison is maintained with the Colorado Department of Rehabilitation. A number of rehabilitation patients are referred to this agency in order to arrange enrollment in community courses. This agency assists the patient in filing his application for support of training with the state in which the patient has residence. A counselor from the local state agency attends rehabilitation conferences and provides direct assistance to our patients in working out training and if necessary, job placement. Thus, "complete rehabilitation" is possible during hospitalization.

Illustrative Case Study of "Total Rehabilitation"

A 30 year-old white married woman was referred to National Jewish Hospital in February, 1955, by the medical director of a hospital at which she had been a patient, intermittently, since 1952. Three months after her first hospitalization, she left the

hospital against medical advice. In 1953, she was hospitalized. Right posterolateral thoracoplasty was performed in 1954. Her sputum remained highly positive and roentgenograms revealed a large cavity with a fluid level under the thoracoplasty, and a cavity on the left.

She was an attractive woman who had been separated from her husband for five years. A daughter born in 1945 and a son in 1948 were being cared for by her husband's family. Her parents were deceased.

At the time of admission to National Jewish Hospital, the patient's condition both physically and emotionally was poor. She was depressed and extremely concerned about her future. She was seen on a regular basis by a staff social worker. Occupational therapy was provided on the ward, except for those rare times when she was able to go to the clinic. With a great deal of help on the part of the medical and rehabilitation staffs, she eventually was able to undergo four separate surgical procedures during 1955 and 1956. In spite of the first three surgical procedures, the sputum remained persistently positive, she lost weight, and deformity increased. She expressed extreme anxiety before each operation and obviously was greatly concerned about her increasing physical deformity. She expressed fear of being hurt, was concerned about dying and became depressed after each surgical procedure.

During this period, she was preoccupied with her physical condition to the point of showing only slight interest in planning for the future. However, in late 1955, for the first time, she expressed an interest in cosmetology.

During 1956, the patient began to discuss her feelings about her family. Her intense feelings of dependency and insecurity gradually emerged. She felt quite guilty about not being able to care for her children, even though she recognized that physically she was not able to earn a living at that time. With casework help she was able to keep her anxieties under control.

By the early part of 1957, her sputum had become consistently negative on culture. Only then did she turn her attention to vocational planning. The social worker referred her for vocational evaluation. After completion of vocational testing and counseling, she was assigned to both the cosmetology and clerical programs in the hospital. A test period in the hospital's beauty shop confirmed her interest and aptitude for further training in cosmetology. She was then placed in a cosmetology program in a local accredited training center. However, since some reservations had been held concerning her physical ability to meet the demands of a full-time program, this was planned as part-time training.

She began formal training in September, 1957. Immediately, she began to gain weight and her general physical condition improved. She seemed to gain a great deal of satisfaction from this program and her physical stamina seemed to justify a change. Shortly thereafter she was placed on full-time training status. Social service and vocational counseling assistance were continued throughout this period. She completed her State Board Examination in June, 1959. As a result of her excellent school record, she had several job opportunities available to her. She was discharged from the hospital in July, 1959. During the entire training period, she resided in the rehabilitation dormitory.

At the time of discharge, she was very pleased with herself. She was particularly happy to be able to work and help support her children. By this time she seemed rather definite about not returning to her husband. She appreciated her in-law's care of her children, and since her husband did not live with his family, she planned to spend some time with her in-laws and the children in order to become reacquainted with them. Initially, she planned to leave the children with her in-laws until she started to work, located an apartment, and saved some money. In time, she planned to establish a home for herself and her children.

An individual, once considered a hopeless case and doomed to remain hospitalized for the rest of her life was restored to a productive existence by a combined medical-rehabilitation program. The road to rehabilitation was long and difficult and the patient had to be helped all along the way, but the results were rewarding to the staff, the community, and most of all to the patient herself.

There are many other patients with problems as difficult as this one. While this case represents a long-term rehabilitation problem, the total team approach applied in this instance is representative of the program that has been available to all of our patients on an individual basis, regardless of the extent of their illness. Through this approach we may provide maximum opportunity for rehabilitation to a greater number of people who are hospitalized with tuberculosis.

SUMMARY

It seems fair to assume, on the basis of several years of preliminary experience, that a modern treatment program for tuberculosis should combine the effective use of all aspects of medical treatment, especially chemotherapy, early ambulation, and planned activity. It was observed that this program which emphasized the healthy aspects of the patient's emotional and social adjustment often served to counteract any tendency to become dependent upon the hospital. Vocational training, equipment, and prescribed physical activity were not considered enough. It was noted that the rehabilitation program became moré effective when patients realized that they were being offered a real opportunity to be helped emotionally, socially, and/or vocationally.

It is our conclusion that it is not useful to employ the concept of the "typical" tuberculous patient. Attempts to understand tuberculous patients in terms of stereotypes can often be misleading.[7,8] Rehabilitation planning should, therefore, be geared to meet the unique needs and personality differences of individual patients. This necessitates close cooperation between all members of the staff so that every aspect of the patient's life can be considered as part of "total treatment." Such a rehabilitation program as is described here seems to offer the best opportunity to prepare the hospitalized patient to return home as a productive citizen and with a greater degree of security.

Many of the barriers, which for so many years limited the scope of rehabilitation, have been removed under this approach. Should the results of this program be confirmed by careful follow-up studies, it is fair to conclude that we have entered a new era in the rehabilitation of tuberculous patients.

RESUMEN

Parece justo asumir, basandose en varios años de experiencia preliminar, que los planes para el tratamiento moderno de la tuberculosis deben combinar el uso efectivo de todas las modalidades del tratamiento médico, especialmente de quimioterapia, ambulación temprana, y actividad planeada. Se observó que este plan que destaca los aspectos saludables de la adaptación social, emocional y social del enfermo a menudo sirvieron para contrarestar cualquier tendencia del paciente a depender del hospital. Adiestramiento vocacional, equipo, y actividad física prescrita no se consideraron suficientes. Se noto que los planes de rehabilitación se hicieron mas efectivos cuando los enfermos se daban cuenta de que se les ofrecía una verdadera oportunidad ayudandolos emocional social y vocacionalmente.

Nuestra conclusión es que no es útil emplear el concepto de enfermo de tuberculosis "tipico." Los intentos para comprender a los enfermos de tuberculosis en forme estereoatipada son erróneos frecuentemente.

Al planear la rehabilitación, por tanto, debe procederse a atender a las necesidades individuales y a las diferencias individuales de cada enfermo. Esto requiere cooperación estrecha entre todos los miembros del personal de manera que cada parte de la vida del enfermo se puede considerar como parte del "tratamiento total." Tal programa parece o ofrece la mejor oportunidad para preparar la vuelta del hopitalizado a su hogar como ciudadano util y con mayor seguridad.

Muchos de los obstaculos que se han opuesto por muchos años a la amplitud de la rehabilitación se han quitado de esta menera. Si esto se confirma por estudios seguidos por largo tiempo puede decirse que se ha entrado en una nueva era en la rehabilitación de los tuberculosos.

RESUMÉ

Il semble logique d'assurer, sur la base de plusieurs années d'expérience préliminaire, qu'un programme de traitement moderne pour la tuberculose devrait associer l'utilisation effective de tous les aspects du traitement médical, particulièrement la chimiothérapie, la mobilisation précoce et l'activité dirigée. On a observé que ce programme, qui met l'accent sur les aspects sains de la condition émotionnelle et sociale du malade, a souvent permis d'ampêcher sa tendance a devenir dépendant de l'Hôpital. Un entrainement professionnel, un équipement, et la prescription d'une activité physique ne sont pas considérés comme suffisants. Il a été noté que le programme de réadaptation devenait plus efficace lorsque les malades prenaient conscience qu'on leur offrait une occasion réelle d'être aidés émotionnellement, socialement et/ou professionnellement.

C'est la conclusion de l'auteur qu'il n'est pas utile d'employer le concept de malade tuberculeux "typique." Des tantatives pour comprendre lcs malades tuberculeux selon des termes stéréotypés peuvent souvent conduire à une impasse. Un Programme de réadaptation devrait donc être conçu pour aller au-devant des besoins individuels et des différences de personnalités des malades. Ceci nécessite une collaboration étroite entre tous les membres du personnel de telle sorte que chaque aspect de la vie du malade puisee être considéré comme une partie d'un "traitement global." Un tel programme de réadaptation comme il est décrit ici, semble offrir la meilleure occasion de préparer le malade hospitalisé au retour dans son foyer comme un citoyen productif et avec un plus grand degré de sécurité.

Beaucoup des barrières qui pendant tant d'années limitèrent le champ de la réadaptation, ont été abaissées sous cette tentative. Même si les résultats de ce programme

devaient être confirmés par des études systématiques soigneuses, il serait logique de conclure que nous sommes entrés dans une nouvelle ère dans la réadaptation des malades tuberculeux.

ZUSAMMENFASSUNG

Es dürfte recht und billig sein, auf der Grundlage mehrjähriger vorläufiger Erfahrung als erwiesen anzusehen, daß ein moderner Behandlungsplan für die Tuberkulosen den effektiven Wert aller Aspekte interner Behandlung, besonders der Chemotherapie, frühzeitiger Übernahme in ambulante Behandlung und schrittweisen Tätigsein miteinander verbinden muß. Es wurde bemerkt, daß dieses Programm, das die gesundheitsfördernden Seiten der gefühlsmässigen und sozialen Anpassung des Patienten unterstreicht, oft dazu diente, jegliche Tendenz, vom Krankenhaus abhängig zu werden, zu vereiteln. Berufliches Training und Rüstzeug sowie körperliche Aktivität nach ärztlicher Verordnung wurden nicht genügend in Betracht gezogen. Es wurde festgestellt, daß das Programm der Rehabilitation wirksamer ausfiel, wenn dem Kranken klar wurde, daß man ihm eine wirkliche Gelegenheit zur geistigen, sozialen und/oder beruflichen Hilfe bot.

Wir sind zu der Überzeugung gelangt, daß es nicht dienlich ist, den Bergriff des "typischen" tuberqulösen Patienten zu verwenden. Bemühungen, den tuberkulösen Patienten mit Hilfe von stereotypen Ausdrücken zu erfaßen, können oft in die orre führen. Pläne zur Rehabilitation sollten daher so zum Zuge kommen, daß sie den jeweiligen besonderen Bedürfnissen und persönlichen Eigenschaften des einzelnen Kranken entgegen kommen. Das erfordert enge Zusammenarbeit aller Mitglieder des betreffenden Kollegiums, daß jede Seite des Lebens des Patienten als Teil der "totalen Behandlung" berücksichtigt werden kann. Ein solches Programm für die Rehabilitation, wie es hier beschrieben wird, scheint die beste Möglichkeit zu gewähren, um den in der Anstalt untergebrachten Patienten vorzubereiten auf die Rückkehr nach Hause in Form eines produktiven Bürgers und mit einem größeren Maß von Sicherheit.

Viele der Hindernisse, die während so vieler Jahre den Bereich der Rehabilitation eingeengt haben, wurden bei dieser Betrachtungsweise aus dem Weg geräumt. Würden die Ergebnisse dieses Programms durch sorgfältige Verlaufsbeobachtungen bestätigt, so wäre der Schluß angemessen, daß wir in eine neue Phase in der Rehabilitation des tuberkulösen Patienten eingetreten sind.

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ERRATUM

The correct title of the paper by Maurice S. Tarshis, Ph.D., Alexandria, Louisiana, which appeared in the October, 1961 issue of *Diseases of the Chest* (40:374) is "Further Investigation on the Usefulness of the Direct Qualitative Micro-Niacin Test for Distinguishing Human Tubercle Bacilli from Other Mycobacteria."

The Use of Hypertonic Aerosol in Production of Sputum for Diagnosis of Tuberculosis*

Comparison with Gastric Specimens

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Although radiologic characteristics and tuberculin positivity are important, proof of the diagnosis of pulmonary tuberculosis depends upon demonstration of tubercle bacilli in bronchial secretions. Failure to recover tubercle bacilli may leave sufficient doubt of the validity of the diagnosis to diminish the physician's vigor in pursuing and the patient's willingness to accept treatment. When the patient is actively producing sputum or when disease is extensive, little difficulty is encountered. However, 30 per cent of the patients admitted to the diagnostic ward of our Tuberculosis Section are unable to produce adequate sputum for bacteriologic study. Many of these have minimal lesions and present diagnostic problems. Traditionally, the early morning gastric aspiration has been utilized in such cases, but even with multiple specimens, the diagnostic yield is low (less than 50 per cent).

Bickerman, Sproul and Barach[1] described a method utilizing a heated hypertonic aerosol in obtaining sputum for cytologic diagnosis of lung cancer. They were able to collect adequate sputum specimens in a significant number of subjects without evidence of pulmonary disease and with no cough or sputum. This report suggested that similar methods might be of value in the bacteriologic diagnosis of tuberculosis and stimulated the present study.

Material

During the period of the study (May, 1959 - October, 1960), 171 male patients were admitted to the diagnostic ward of the Tuberculosis Section. Criteria for admission to the study were: (1) no previous bacteriologic diagnosis of tuberculosis and, (2) absence of spontaneous cough or sputum production. Fifty-two patients met these criteria, 13 of whom were eventually found to have either inactive disease or nontuberculous lesions. The remaining 39 patients were diagnosed as having active tuberculosis and are the subject of this report. Extent of disease

TABLE 1—COMPARISON OF CULTURAL RESULTS OF INDUCED SPUTUM AND GASTRIC SPECIMENS (39 CASES OF TUBERCULOSIS)

Type of Specimen	Number of Patients	Culture Positive	Total Specimens	Culture* Positive
Gastric	37	16 (43 per cent)	108	30 (28 per cent)
Sputum	31	20 (65 per cent)	89	47 (53 per cent)

*Difference significant (p+.0002)

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(Presented in part at the Fourth Annual Meeting, Society of Air Force Internists and Allied Specialists, USAF Hospital Lackland, Lackland Air Force Base, Texas, 2 February 1961.)

was minimal in 18, moderately advanced in 18, and far advanced in one. A patient with tuberculous pleurisy and one with renal disease, but without evidence of pulmonary disease, is also included.

Methods

A heated nebulizer which delivers a liquid and vapor mist at a temperature of approximately 105°F. was used. A solution of 10 per cent sodium chloride in 20 per cent propylene glycol was nebulized either with oxygen at a flow rate of 7 liters per minute, or with an electric diaphragm air compressor as the propellent. The patient was instructed to inhale the aerosol mist from a distance of four to six inches from the outlet of the nebulizer. All material coughed up during and for one hour after a 20 minute period of nebulization was collected and this was repeated approximately four to six times during the day. The pooled specimen was submitted to the laboratory. In each case, gastric specimens were obtained on three successive days, followed by three successive days of induced sputum collection. Later in the study, the saline content of the solution was reduced to 5 per cent in an effort to avoid clogging of the jets of the nebulizer. A minimum of 5 cc. of total collected sputum was considered adequate. Cultures were processed by standard methods' and cultured in duplicate on Lowenstein-Jensen and Middlebrook 7H1C media.

Results

One or more adequate gastric specimens were obtained in 37 of the 39 patients, yielding positive cultures in 16 individuals (43 per cent). One or more adequate sputum specimens were obtained in 31 of these individuals with positive cultures in 20 cases (65 per cent). All together, a total of 108 gastric specimens were collected, 30 of which were positive on culture for *M. tuberculosis* (28 per cent). Of 89 sputum specimens, 47 yielded positive culture (53 per cent). (Table 1).

Direct comparison of induced sputums and gastrics in the same patients was not possible in all cases because of inability to obtain either adequate gastric specimens or to induce adequate sputum. However, 28 patients produced two or more adequate specimens by both methods. Thirteen of these 28 patients yielded positive cultures by both methods. In six individuals, positive induced sputum cultures were obtained, but all gastrics were negative, and in one individual, a single gastric specimen was postive and all sputum specimens were negative on culture. Thus, 19 patients (68 per cent) were bacteriologically positive for acid-fast bacilli by induced sputum, whereas only 14 patients (50 per cent) yielded one or more positive gastric specimens. In this group of paired specimen patients, 25 of 83 gastric specimens yielded tubercle bacilli

TABLE 2—COMPARISON OF CULTURAL RESULTS IN "PAIRED" SPECIMENS FROM 28 PATIENTS

Type of Specimen	Cases Positive	Specimens	
		Total	Positive*
Gastric	14 (50 per cent)	83	25 (30 per cent)
Sputum	19 (68 per cent)	81	43 (53 per cent)

*Difference significant (p+.002)

(30 per cent), whereas 43 of 81 induced sputum specimens yielded tubercle bacilli on culture (53 per cent) (Table 2). It is of additional interest that smears of sputum concentrate were positive for acid-fast bacilli in six individuals.

Discussion

It would seem logical that material collected directly from the bronchi would contain more viable organisms than would bronchial secretions which have traversed the bronchial tree, the hypopharynx, the esophagus, and have been diluted and digested by gastric juices, and it is generally conceded that sputum is superior to gastric aspirate for bacteriologic study in suspected pulmonary tuberculosis. Some have contended that with careful indoctrination, all patients can be taught to produce sputum. While this is possible in many cases, the degree of success depends upon the zeal and enthusiasm of physician and attendants and upon the cooperation of the patient. Many such "forced" sputa are in reality saliva and of little value. Tracheal lavage and laryngeal swabs have met with some success, but in general have no advantage over gastric aspiration. Tracheal lavage requires experience and skill and the explosive cough produced is a hazard to the operator. Laryngeal swabs have not been found to be as adequate as gastric specimens.[3,4] Bronchial washings at time of bronchoscopy and postbronchoscopy sputum will occasionally yield positive cultures, but obviously these techniques are not applicable as routine diagnostic measures.

Nebulization of isotonic solutions at room temperature produces aerosols which are 30 to 60 per cent of humidity of saturated air at body temperature. By raising the temperature to 100-105°F. and by increasing the tonicity of the nebulized solution, it is possible to get aerosols which are at or above body humidity. At increased temperature, the air will hold more water vapor and the higher tonicity lowers the vapor pressure of the droplets, reducing their tendency to vaporize. These droplets are then carried to the lower respiratory tract where they are deposited. The hypertonic solution has a mildly irritating and an osmotic action in the smaller bronchi and bronchioles, producing cough and sputum. The warm aerosol does not have the irritant effect of a cold hypertonic aerosol on the pharynx and upper respiratory tract, and thus premature cough is avoided.

Barach, *et al.*,[1] and subsequently others[5,6] have demonstrated that inhalation of hypertonic aerosol will yield adequate specimens for cytologic study in up to 86 per cent of subjects with no cough or sputum. In our total group of 52 patients, suitable sputums were obtained in 44 (85 per cent). Most of the failures occurred early in the study, and although in a few cases poor patient cooperation may have played some role, inadequate instruction and inexperience was undoubtedly the major factor affecting success. Five failures occurred in the first ten patients admitted to the study, and only four in the subsequent 42. Patient acceptance has been excellent as compared to gastric lavage.

One question in our minds at the onset of the study was whether the composition of the aerosol would interfere with the ability of tubercle bacilli to grow out in culture. The relatively high percentage of positive cultures obtained indicates that the solution does not affect the viability of tubercle bacilli in the resultant sputum.

Some problems have been encountered in the use of apparatus. Frequent occlusion of the jets resulted in maintenance problems. This was not greatly affected by reducing the concentration of saline to 5 per cent. Careful cleansing and flushing of the apparatus with alcohol after each use has minimized this problem. A greater problem has been short effective life of the heating elements, with delay in obtaining replacement parts. Clearly, a more durable element is needed to make the apparatus more serviceable.

From a diagnostic standpoint, induced sputa appear to be superior to gastric specimens in this group of patients. The series is small, however, and the increased numbers of patients with positive sputum diagnosis falls short of statistical significance. The relative percentages of sputum specimens versus gastric specimens yielding positive cultures reveal a significant superiority to the induced sputum (p= less than .002). To date, only in-patients have been studied. Future study will be directed to comparison of a single-sitting collection of induced sputum with gastric cultures to determine the applicability of this technique to out-patient use.

SUMMARY AND CONCLUSIONS

Sputum induced by inhalation of a heated hypertonic aerosol yielded a greater number of cultures positive for tubercle bacilli than did gastric specimens from the same group of in-patients under investigation for tuberculosis. The method appears to have value in the diagnosis of inflammatory disease of the lung and deserves further study.

RESUMEN

El esputo provocado por la inhalación de un aerosol calentado hipertónico produjo un mayor número de cultivos positivos para el bacilo de la tuberculosis que los especí-

menes de contenido gastrico en el mismo grupo de enfermos internados en los que se investigó tuberculosis. El método parece tener valor en el diagnóstico de enfermedad inflamatoria del pulmón y merece mayor estudio.

RESUMÉ

Des crachats provoqués par une inhalation d'un Aérosol hypertonique chaud donnaient en plus grand nombre des cultures positives pour le bacille tuberculeux que les tubages gastriques dans un même groupe de malades hospitalisés en hue de préciser le diagnostic de tuberculose. Cette méthode paraît avoir de la valeur pour établir le diagnostic des infections pulmonaires et mériterait une étude plus poussée.

ZUSAMMENFASSUNG

Die durch Inhalation des erwärmten hypertonischen Aerosols bewirkte Sputumproduktion fuhrt bei der Untersuchung auf Tuberkelbakterien zu einer grösseren Anzahl positiver Kulturen, als die Untersuchung des Magensaftes bei der gleichen stationär behandelten Patientengruppe. Die Methode erscheint wertvoll bei der Diagnose entzündlicher Lungenerkrankungen und verdient weitere Untersuchungen.

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ATRIAL INFARCTION OF HEART

A clinical diagnosis of atrial infarction should be suspected in patients with ventricular myocardial infarction having any form of atrial arrhythmia. Frequent electrocardiograms should be obtained, especially if sinus rhythm has just been re-established after episodes of supraventricular tachycardia or atrial fibrillation.

The major electrocardiographic criteria for the diagnosis of atrial infarction are as follows: elevation of the P-Ta segment of over 0.5 mm. in V_6 and V_6 with reciprocal depression of the same segment in V_1 and V_2; elevation of the P-Ta segment of over 0.5 mm. in lead I and its depression in leads II or III; depression of the P-Ta segment of more than 1.5 mm. in precordial leads and 1.2 mm. in leads I, II, and III in the presence of any form of atrial arrhythmia.

The minor electrocardiographic criteria in making the diagnosis of atrial infarction are as follows: abnormal P waves: M-shaped, W-shaped, irregular or notched; depression of the P-Ta segment of small amplitude without elevation of this segment in other leads cannot be regarded by itself as positive evidence of atrial infarction.

A diagnosis of atrial infarction can sometimes be made when the presence of ventricular myocardial infarction cannot be definitely established by electrocardiogram.

The treatment of atrial infarction is similar to that of ventricular infarction. Attention should be directed to the control of atrial arrhythmias and to the prevention of mural thrombi.

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Aortic Body Tumors*

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Aortic body tumors, though comparatively rare, nevertheless have a place in the differential diagnosis of intrathoracic tumor. A review of the literature reveals ten previous case reports beginning with Lattes' two cases in 1950.[2,6,7,8,10-12,14]

This type of tumor has variously been referred to as a non-chromaffin paraganglioma,[9] chemodectoma,[4,6,11] and aortic body tumor.[3] Lattes[8] suggested the term "non-chromaffin paragranuloma," and de Castro[4] the term "chemodectoma." The latter is a term describing the tumor on the basis of function (of the aortic body). Each of the terms would appear equally appropriate to describe this group. The other functionally related tumors include those of the carotid body, the *glomus jugulare, paraganglion tympanicum,* and *paraganglion intravagale.*

Function of Chemoreceptor Tissue

Comroe,[5] and Dripps and Comroe[5] have pointed out that the chemoreceptor mechanism responds to a decrease in oxygen tension, to a decrease in pH of the plasma, and to an increase in the temperature of the blood. The vagus nerve transmits these impulses to the medullary vasomotor and respiratory centers.

Anatomic Location of Chemoreceptor Bodies

The usual anatomic position of the chemoreceptor bodies has been described by Comroe,[5] Dripps,[5] Hollinshead,[9] and Barnard.[1] Aortic bodies are situated on the anterolateral portion of the left aortic arch near the origin of the left subclavian artery, near the innominate artery either lateral to the right subclavian artery or close to the bifurcation of the subclavian and common carotid artery, near the pulmonary end of the ductus arteriosus, or on the right side on the surface of the pulmonary trunk; and in an area adjacent to the ascending aorta and the left coronary artery.

Location of Reported Tumors

The following are the reported anatomic locations in which tumors have arisen: (1) the immediate vicinity of the aortic arch and innominate artery;[9] (2) in the adventitia of the aortic arch near the obliterated ductus arteriosus;[9] (3) anterolateral aspect of the right lower lobe of the lung;[7] (4) the left subclavian artery,[12] and on the artery immediately distal to the thyrocervical axis and completely encircling the artery;[10] (5) the right posterior costovertebral sulcus,[6] and the sulcus at the ninth to 11th rib related to the descending aorta on the right;[6] (6) right posterior mediastinum;[11] (7) between the lobes of the left lung;[14] (8) questionable right hemithorax adherent to the diaphragm;[14] and (9) anterior aspect of pericardium overlying the right atrium.[3]

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Case Report: Mrs. E. M. was a 28 year-old housewife who appeared to be an unusually emotionally labile individual. She had had anorexia and insomnia for years and for the last five to six months had had vomiting attacks, sometimes daily, sometimes weekly. There was a history of an automobile accident one year prior to hospital admission when she sustained a deep laceration of the left shoulder and developed chest pain which cleared over a period of several months.

On physical examination, the blood pressure was 115/60 in the left brachial artery and 120/80 in the right. Pulse was regular sinus rhythm, good volume. The brachial pulses and femoral pulses were equal bilaterally. The trachea was mid-line and the lungs were clear to auscultation and percussion. There was no clubbing, no cyanosis, the liver was not palpable, and there was no elevation of the jugular venous pressure. There was a keloid scar over the left shoulder at the base of the left neck. There was no murmur auscultated over the precordium and no evidence of cardiac abnormality. She was a moderately thin woman in no immediate distress. X-ray film of the chest (Fig. 1) February 26, 1960, revealed a 4 x 5.8 cm. mass off the left margin of the aortic arch apparently being adjacent to or in the wall of the aorta in the area of the left subclavian artery or immediately below it.

On March 9, 1960, the left hemithorax was explored through a posterolateral thoracotomy utilizing the rib bed beneath the inferior margin of the fifth rib. A smooth rounded extrapleural mass 6 cm. in diameter was found overlying the posterolateral portion of the aorta beginning 1 cm. below the origin of the left subclavian artery. Its surface was coursed with many venous radicals and in its entirety lay subpleurally. Utilizing sharp dissection the tumor was dissected from off the aorta and reflected posteriorly. There were numerous large vascular and nervous tissue communications, the latter appeared to be continuous with a large and distorted sympathetic chain. There were many frank nervous tissue communications in this area and the chain itself appeared to be more or less a thick network of nervous tissue strands. The impression at operation was that this represented a neurogenic tumor. It appeared to be encapsulated and was not believed to be malignant. Postoperatively she convalesced without event and six months postoperatively there was no evidence of recurrence.

Gross pathology of the specimen: The specimen consisted of a moderately firm ovoid, somewhat resilient lesion 5 cm. in maximum dimension. Externally it was slightly lobulated, well encapsulated and red-tan. Sections showed a homogenous gray-pink to red-brown, smooth surface with a centrally located dark brown 0.8 cm. hemorrhagic area of discoloration. The lesion was surrounded by a 1 mm. gray capsule.

Microscopic examination: The tumor was composed of large polyhedral cells which tended greatly to reproduce the architecture of a normal aortic body except there was greater variation in size and shape of cells than in the normal organ. The tumor cells were arranged in nests (Zellballen), and between the latter there were fibrous septa rich in capillaries. No mitotic figure was seen. The tumor cells were oval, vesicular,

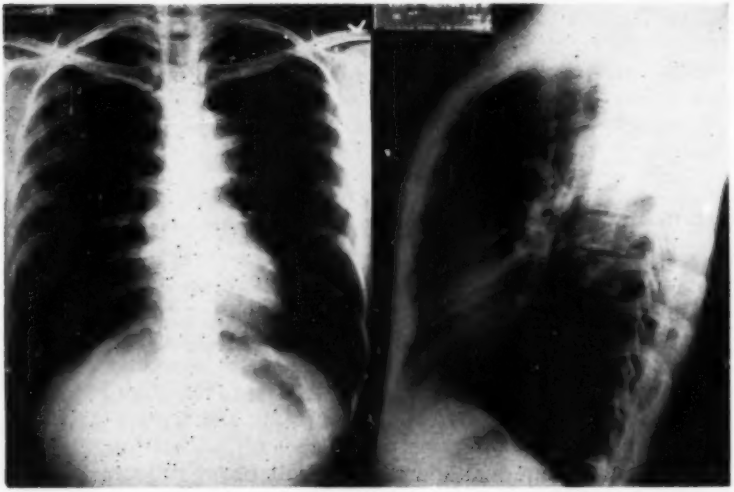

FIGURE 1A FIGURE 1B

FIFURES 1A and 1B: Preoperative x-ray films of the chest revealed a 4 x 5.8 cm. mass which could not be separated from the left margin of the aortic arch.

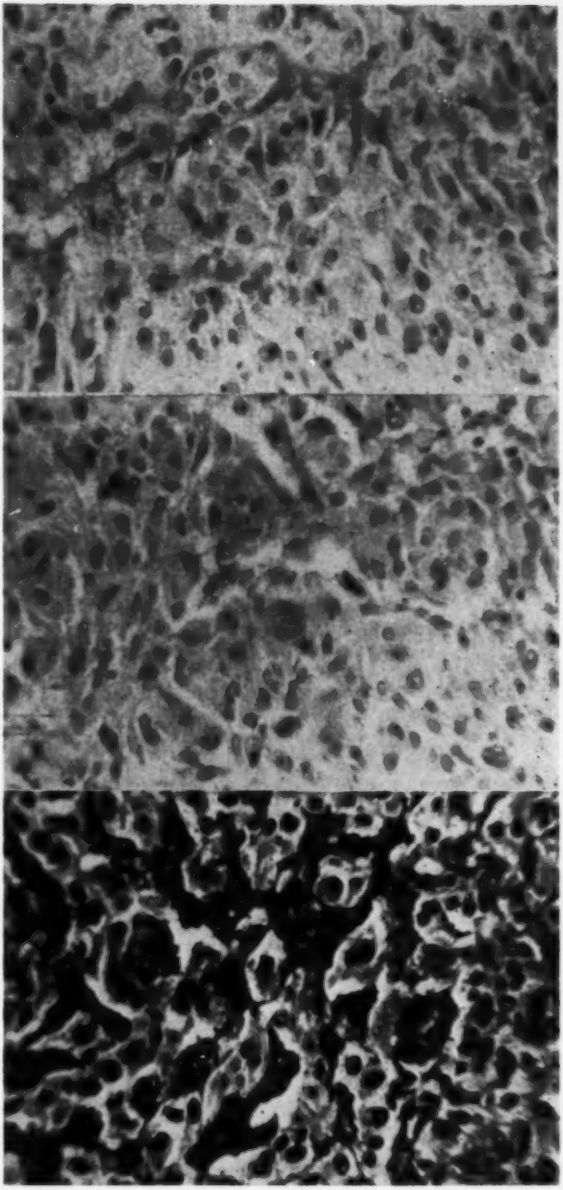

FIGURE 2

FIGURE 3

FIGURE 4

FIGURE 2 (upper): The tumor cell arrangement is one of nests of cells, separated in part by fibrous connective tissue septa rich in capillaries. FIGURE 3 (center): The individual tumor cells are uniform in size and shape, plump in configuration, and contain oval to round, even-sized vessicular nuclei. FIGURE 4 (lower): The nests of tumor cells are clearly seen and are separated by the darker staining reticulum of the fibrous septa.

central or slightly eccentric nuclei with a fine minutely stippled chromatin pattern. The nucleoli were solitary, small, and often eosinophilic (Figs. 2 and 3). The cytoplasm of each cell was abundant, clearly outlined, finely granular and eosinophilic. Reticulum stain (Fig. 4) brings out the typical cellular nests of the tumors cells.[12] Microscopic sections of the lesion were reviewed by Dr. Malcolm B. Dockerty of Rochester, Minnesota, who concurred in the diagnosis of chemodectoma.

Treatment

The treatment for these tumors has been surgical excision with deep x-ray on occasion for recurrence and for apparent metastasis. In Perasolo's[14] case, a "fist sized" tumor was excised between the lobes of the left lung. Five and one-half years later a second tumor the size of a "child's head" was excised from off the right hemidiaphragm. Later a questionable metastasis to bone was treated with deep x-ray.

Of Duncan's[6] two cases, the first had a 6.4 cm. mass removed from the right posterior portion of the thorax adjacent to the ninth and tenth thoracic vertebrae with erosion of the tenth rib. Fourteen years after operation and removal of the tumor his second case developed a tumor in the vertebral column which led to spastic paraplegia of both lower extremities. This recurrence, if it was such, was not biopsied and thus the histology of the recurrence is not available.

Monroe's[13] case was a 22 year-old man who was given deep x-ray over the tumor mass in the left subclavian region on two occasions (receiving 400 r the first time) without response. It is stated that he deteriorated over the next four years developing liver and probably lung metastasis.

In MacDonald's[10] case, a 79 year-old man was found to have an incidental aortic body tumor about the left subclavian artery located immediately distal to the thyrocervical trunk. There was no connection at the carotid artery or the vagus nerve.

Gillis'[7] case was treated surgically with the tumor in the right lower lobe, removed by lobectomy. Two years postoperatively there was a recurrence in the wound. This was excised, but it recurred again, growing at such a rate that it was considered inoperable when next seen. It was treated with the cobalt bomb without response. The patient died.

Lattes'[9] first case was a 59 year-old man with a mass in the right side of his neck behind the right lower sternomastoid muscle extending beneath the right clavicle, with a mediastinal mass displacing the trachea and esophagus to the left. The cervical portion was removed from above and one month later the thoracic portion was explored and found not resectable. The tumor was well encapsulated below and intimately associated and connected with the innominate artery and the internal jugular vein. The tumor was essentially intrathoracic. Lattes' second case was a man who died from bulbar poliomyelitis. At necropsy, a 2 cm. carotid body tumor was found at the bifurcation of the carotid artery, a chemodectoma found in the vagus nerve in the region of the styloid process at the base of the skull (ganglion nodosum), and a one and one-half cm. aortic body tumor found at the site of the obliterated ductus arteriosus, loosely attached to the adventitia.

McDonald's[11] case report dealt with a 38 year-old woman with a contiguous superior mediastinal right neck mass. It was removed via a collar incision, its weight was 70 gm., and it was encapsulated and fixed posteriorly in the region of the vertebra. It was believed benign.

ACKNOWLEDGMENT: I wish to thank Dr. Malcolm B. Dockerty for his opinion regarding the diagnosis, and Dr. Royal B. Lea for his help with the reported case.

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CORONARY ANGIOGRAPHY

Bjork and Hallén report a modified method of coronary angiography originally introduced by Arnulf and Chacornac with cardiac arrest induced by acetylcholine for clinical use. A small dose of acetylcholine is placed in the catheter, the tip of which is placed in the ascending aorta near the aortic valve. When the contrast medium is injected through the catheter, it pushes the acetylcholine into the coronary circulation. Cardiac arrest is induced within one to two seconds. The length of the cardiac arrest is easily controlled with the help of atropine sulphate, which is injected through the catheter into the coronary circulation. The method has been applied to patients with severe angina pectoris. Coronary angiography during cardiac arrest with the very low systemic flow and with x-ray exposure in one plane gives radiograms with very good clarity and of high quality.

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THE DIAPHRAGM IN PRIMARY LUNG CANCER

The authors examined changes in the position and structure of the diaphragm in primary lung cancer and investigated their relation with the type of growth of carcinoma and with the functional condition of the lung.

In the instances where the diaphragm appeared to be elevated, three different anatomo-histologic situations were observed. In a first group, atrophy of muscle bundles and its replacement by connective tissue were observed. It was carcinomatous infiltration of the phrenic nerve. The lung parenchyma maintained sometimes its complete ventilation.

In some other cases, atrophy or connective tissue substitution resulted from direct invasion of the muscle by the new growth or by compression of nerve fibers in the muscle. In this second group, infiltrative spread of cancer from the hilum was also observed.

In a third group, including one large nodular cancer and one of the massive type, the diaphragm conserved its complete structural integrity; its elevation was in close relation to the appearance of hypoventilation and atelectasis of the lung.

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A Case of Tuberculous Thoracic Aortitis with Massive Hemoptysis Resulting from Rupture of Involved Aorta into Lung*

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It is generally accepted that tuberculous lesions are rarely found in the wall of the aorta. Wettland and Scott[1] (1956) reported a case of tuberculous false aneurysm of the aorta with rupture into the bronchus. According to their study, tuberculous aortic perforation into the respiratory tract had only occurred in four previously published cases. Prior[2] (1955) also reported a case with tuberculous periaortitis from caseous lymphadenitis resulting in rupture of the aorta into the left main bronchus. Such a case has never been reported in Japanese literature. The present report is of a case of tuberculous thoracic aortitis. The patient died of massive hemoptysis which resulted from the rupture of involved aorta into the right lung.

Case: F.T., a married woman, 28 years old. History: She had been quite well and tuberculin cutaneous test had been negative until she married in 1949 when she was 21 years old. She had pleuritis and endometritis tuberculosa at the age of 22 years. After treatment with streptomycin and para-aminosalycilic acid for about two years, she gradually recovered. However, endometritis tuberculosa relapsed when she was 25. Chest x-ray film at that time revealed no tuberculous lesion in the lung. Since then, under treatment with antituberculosis chemotherapy, she remained well until July 3, 1956, when she complained of sudden severe pain in the lower abdomen. A diagnosis of acute appendicitis was made by a surgeon and appendectomy was performed on the same date. In the excised appendix, slight inflammation was found. After the operation, continuous fever developed and her body temperature rose to 40°C. on July 14. Since liver abscess was suspected, laparotomy was performed again by the

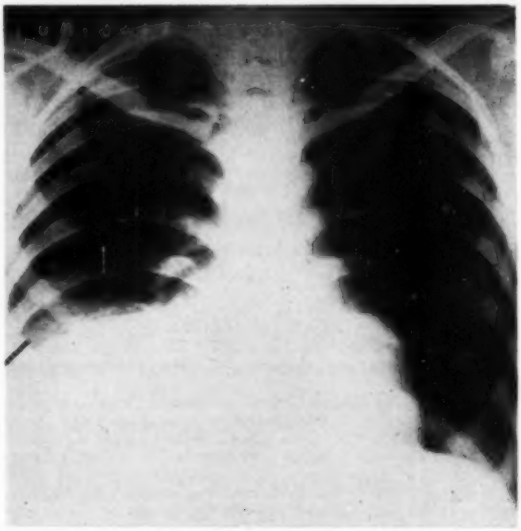

FIGURE 1: Chest x-ray film, showing a diffuse shadow in the lower portion of the right lung and abnormal elevation of the right leaf of the diaphragm.

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same surgeon on July 22. However, no liver abscess was found at the operation, but several tubercles were observed on the surface of peritoneum. Liver and spleen were slightly enlarged. The second operation was an exploratory one. Thereafter, the remittent high fever lasted until September 15, although she had been treated with chloramphenicol and isoniazid. Second chest x-ray film on August 23 revealed no tuberculous lesion. About the end of September, her body temperature dropped to 37°C. spontaneously. A week before admission, she noticed chest pain. She coughed abruptly and expectorated bloody sputum.

She was admitted on October 11, 1956 complaining of hemoptysis, cough and chest pain. Physical examination revealed a well-nourished woman in spite of long-standing fever; body temperature was 38.8°C., blood pressure 120/60, pulse rate 120 with regular rhythm, no jaundice and no abnormal enlargement of lymph nodes. Her tongue and pharynx were normal. On chest examination the lung-liver border was at the fifth rib and abnormal dullness was found over the lower part on the right side of the chest. Respiratory movement of the diaphragm was not observed on the same side. There were no rales. Cardiac dullness was normal, and x-ray film of the chest revealed a diffuse shadow in the lower portion of the right lung and abnormal elevation of the right leaf of the diaphragm, which was considered to be pleural scarring (Fig. 1). No other abnormal shadow was found. On abdominal examination, operative scars were found in the right upper and right lower abdomen, where tenderness was demonstrated. There were no ascites. The liver edge was not palpable because of operative scars. The spleen was slightly palpable. No other abnormality was found in the abdomen. There was no pitting edema. Neurologic examination was normal. Laboratory data: urinalysis revealed + for protein, a few erythrocytes and leukocytes in sediment, occult bleeding test in feces was +++ positive. Blood examination revealed slight anemia (hemoglobin 72 per cent and erythrocyte count 3,410,000) and neutrophilia (adult neutrophiles 78 per cent and band-form 17 per cent), with leukocytosis (leukocyte count 5600). Blood sedimentation rate was 100 mm. per hour. Results of electrophoretic analysis of serum protein were as follows: total protein 6.8 g./dl. albumin 43 per cent, globulin α11 per cent, β13 per cent, γ32 per cent. Serum reactions for syphilis were negative. Cultures of blood were sterile on two occasions. No acid-fast bacillus was demonstrated in smears of bloody sputum microscopically. However, three weeks after her death, three colonies of tubercle bacilli were detected in one month's culture of sputum. Widal's reaction was negative. Bromsulphalein retention was 12.5 per cent after 30 minutes. There were no abnormal findings in ocular fundi.

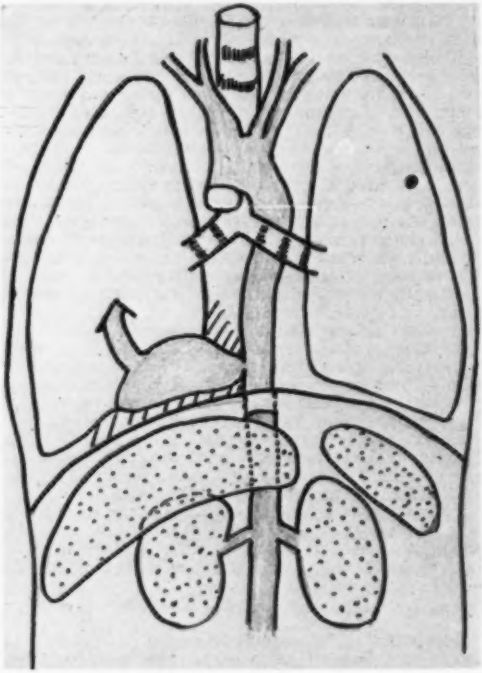

FIGURE 2: Schema of autopsy findings, showing rupture of aorta into right lung and miliary tuberculosis in abdominal organs.

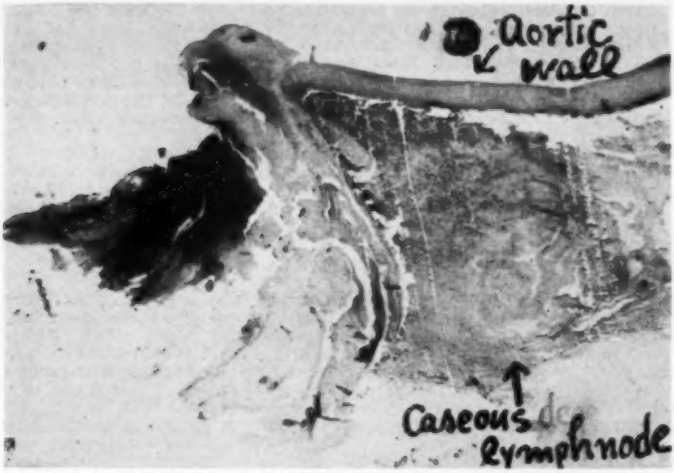

FIGURE 3: Caseous lymph node in periaortic tissue of the ruptured portion.

Course: A diagnosis of chronic septicemia of unknown origin was suspected from the results of clinical examination and laboratory data and she was treated symptomatically. On October 23, 1956, massive hemoptysis took place suddenly and she expired on the same date because of suffocation probably due to aspiration of blood. Necropsy was carried out two hours after death.

Necropsy findings (Fig. 2): Rupture of the thoracic aorta was detected at the site just above the diaphragm. The diameter of the perforation was about 2 mm. The perforation opened into the lower lobe of the right lung through the adhesive pleura and the right lower lung was damaged and filled with coagulated blood. Caseous lymph nodes were found in the periaortic tissue (Fig. 3). Aneurysmatic change of the aorta was not observed. Microscopic examination revealed caseous degeneration in the ruptured portion of the aorta. Although the primary focus for tuberculous infection was found in the upper part of the left lung, no other lesion was found in the lung. Miliary tubercles were observed in some abdominal organs including liver, spleen and kidney. There were numerous tubercles on the surface of the peritoneum too.

Comments: In this case, a diagnosis of chronic sepsis of unknown origin was suspected because of the long-standing remittent fever following the laparotomy, hypergammaglobulinemia, acceleration of blood sedimentation rate and enlargement of spleen, although blood cultures remained always sterile. Since several tubercles had been detected on the surface of the peritoneum at laparotomy, miliary tuberculosis was also suspected as the diagnosis. However, no tuberculous lesion was found in the lung radiologically and high remittent fever did not respond to specific chemotherapy for tuberculosis. These were against making a diagnosis of tuberculosis. The cause of lethal hemoptysis was undetermined clinically and the rupture of tuberculous aorta was never suspected.

Necropsy revealed that this was a case of tuberculosis with multiple lesions. In addition to the initial pulmonary infection, she had suffered from pleuritis, peritonitis or endometritis and died from suffocation caused by massive hemoptysis which resulted from the perforation of tuberculous aortic wall. Although numerous cases with hemoptysis due to aortic rupture have been reported, only a few were due to rupture of tuberculous aortitis. The most common cause of lethal hemoptysis due to rupture of the aorta is syphilitic or arteriosclerotic aneurysm. A few cases of rupture of aorta with tuberculous aortitis have been reported.[1] According to Wettland and Scott, aortic tuberculosis may be classified into two types pathogenetically. One is a bacterial embolization to the intima or the vasa vasorum of the aorta. The other is direct spreading of a tuberculous process from the vicinity of the aorta to the aortic wall. The case reported here seems to belong to the latter. Miliary tubercles found in some organs supplied by the abdominal aorta at necropsy might be formed as a sequel to invasion of tubercle bacilli, which were derived from the lesions of the aortic wall, into the arterial blood.

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Probable Miliary Tuberculosis at Term

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This patient's case history is being reported because of the occurrence of miliary tuberculosis at the time of delivery.

On May 25, 1950, at the age of 18, this white Italian girl was admitted to Monmouth Memorial Hospital in Long Beach, New Jersey, with a diagnosis of "pneumonia." She was found to have left pleural effusion which was aspirated on two occasions. Tubercle bacilli were found in one specimen, but the report was mislaid, and she was discharged improved.

Following this, she noted fatigue and during October, 1950, right pleural effusion was found and she was readmitted to the hospital and acid-fast bacilli were found in the fluid. She was transferred to the New Jersey Sanatorium at Glen Gardner where streptomycin and PAS were administered. She had right thoracentesis on three occasions. Right pneumothorax was started and was maintained for only one month. In March, 1951, she left the sanatorium against advice.

When she returned home, she resumed her full activity against the advice of her physician. During June, 1951, she was found to be pregnant. On December 3, she complained of night cough, and on December 31, 1951, a thorough physical examination was done and a chest x-ray film was taken which was unchanged.

On January 1, 1952, she had vague pains and elevated temperature. She was treated by her physician with an antibiotic without results. That evening, she was admitted to the hospital, and on January 2, had a normal delivery of a baby boy.

During her stay in the hospital, she had persistent low-grade fever. She had persistent cough on discharge from the hospital.

She was readmitted on January 30, when a chest x-ray film suggested miliary tuberculosis. Six weeks later, she was again admitted to the New Jersey Sanatorium when a gastric specimen was found positive for tubercle bacilli. She was treated with streptomycin, PAS and INH and subsequently discharged in good condition.

Her last examination was on October 5, 1960, when she was well and her x-ray film was clear.

Her child is in good health and does not react to tuberculin.

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PROPHYLAXIS OF THROMBOEMBOLIC COMPLICATIONS IN SURGICAL TREATMENT OF PATIENTS WITH MITRAL DISEASE

The authors have used continuous preoperative anticoagulant preparation of patients with mitral stenosis in whom, based on a number of symptoms, intracardiac thrombosis was suspected. This measure helped to reduce the number of fresh thrombi found during the operative procedure in the left auricle and atrium. In 77 patients with heart flutter who had not received anticoagulants, 40 thrombi were found—17 fresh, 17 mixed and 11 organized thrombi. While in 63 patients treated by anticoagulants thrombi were found in 40 patients, they contained three mixed, 37 organized and no fresh thrombi. In these groups of patients the embolic incidence during and after the operation was reduced from eight cases to one case. To prevent the recurrent auricular thrombosis postoperative treatment of patients with anticoagulants is advocated.

Uglov, F. C., and Potashov, L. V.: "Prophylaxis of Thromboembolic Complications in Surgical Treatment of Patients with Mitral Disease," *Chest Surgery (USSR)*, 87.3, 1961.

ELECTROCARDIOGRAM IN MARFAN'S SYNDROME

Sixty-three electrocardiograms from 55 Canadian patients (median age, 18.5 years) with Marfan's syndrome have been studied. Thirty-nine per cent of male patients, 17 per cent of female patients, 23 per cent of patients 20 years of age or younger, and 36 per cent of patients older than 21 years had abnormal tracings. The most common abnormal electrocardiographic pattern (nine tracings from eight patients) was the pattern of left ventricular hypertrophy; this pattern was found in tracings from male patients only. It was thought to reflect left ventricular hypertrophy due to aortic valvular insufficiency. The second most common abnormal electrocardiographic pattern (found in tracings from four male and three female patients) consisted of S-T segment depression or T wave inversion in leads II, III and aVF. This pattern was thought to be a reflection of right ventricular or biventricular hypertrophy, or to be an effect of digitalis. Auricular fibrillation was recorded in two electrocardiograms, incomplete right bundle branch block in seven and complete right bundle branch block in one. There were no other significant disturbances of rhythm or conduction.

From these observations, it was concluded that in this group of patients, Marfan's syndrome is an abiotrophic disorder of the cardiovascular system frequently associated with nonspecific electrocardiographic abnormalities.

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Muco-Epidermoid Tumor of the Bronchus

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As the techniques of pulmonary resection became known and applied, the results of the removal of various pulmonary tumors were compared. The difference in the five-year survival rates of patients with bronchogenic carcinoma and bronchial adenomas was apparent. Geipel, Kramer, Wessler and Rabin made notable contributions in this work.[2,5,10]

However, it was not until 1937 that the differences between the two types of bronchial adenomas were clearly brought forth by Hamperl.[3] The more common variety, the carcinoid adenoma, was first reported by Muller in 1882.[7] These are generally benign and comprise 90 per cent of most series of bronchial adenomas. The less common variety, the cylindroid type, was first described by Heschl in 1877.[4] These lesions account for the remaining 10 per cent and have been more descriptively named adenoid cystic carcinoma. The similarity between this latter type of bronchial adenoma and the counterpart in the salivary and lacrimal glands was sufficient to warrant the name "cylindroma." The term "cylindroma" was first used by Billroth[1] in 1859 to describe a tumor of the orbit and it has been applied to lesions histologically similar in the breast and in the mucous membrane of the mouth and pharynx.

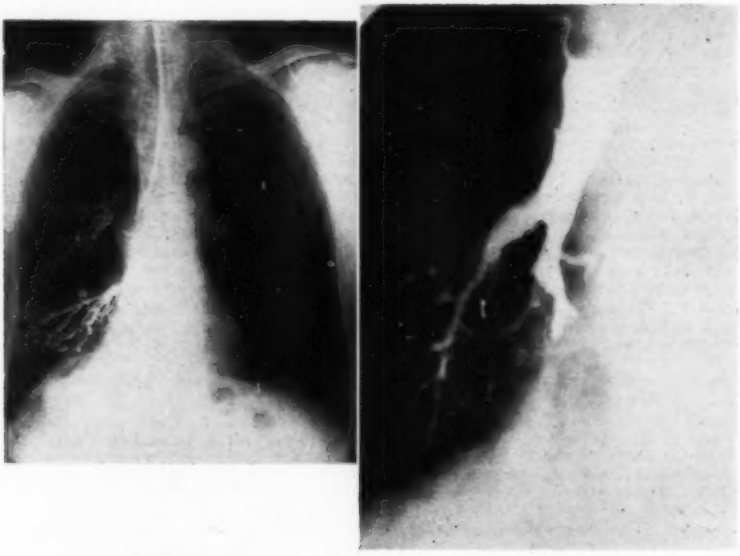

FIGURE 1a FIGURE 1b

FIGURE 1a: Bronchogram shows distortion of right lower lobe bronchi. The lobulated mass can be seen lying on the right diaphragm. FIGURE 1b: Spot film confirms lumen to be obstructed distal to the superior segment orifice.

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It has recently become apparent that included in the cylindromatous classification is a separate type of tumor distinguished both on the basis of histologic differences and on probable clinical course. This type, a muco-epidermoid tumor, was first separated by Smetana of the Armed Forces Institute of Pathology and reported by Liebow in 1952.[8] The term "muco-epidermoid tumor" is in accordance with the muco-epidermoid tumors of the salivary gland described by Stewart, Foote, and Becker.[9] Two cases were described. Grossly these lesions were pedunculated polypoid endobronchial masses which occluded the lumen to varying extent. Microscopically these tumors are covered with metaplastic squamous epithelium. The body of the tumor is composed of a mixture of well differentiated mucous producing cells and sheets of squamous epithelium. Occasionally minimal invasion of local structures is seen.

Four additional cases have been reported by Payne, Ellis, Woolner, and Moersch in their report of 1959.[6] They stressed the fact that symptoms are on the basis of bronchial obstruction and that surgical resection is the only chance for cure. Two of their cases were treated conservatively and died, two weeks and four years respectively after diagnosis. Two underwent pneumonectomy with survivals of at least ten and eight years Because of the location of the lesion, a resection of lesser extent was not feasible. These same authors listed a seventh case of muco-epidermoid tumor mentioned in a personal communication from Liebow.

FIGURE 2a: Muco-epidermoid adenoma obstructing basal segments of right lower lobe.

We would like to present an additional case of muco-epidermoid tumor which produced symptoms of a similar nature, namely bronchial obstruction with distal pulmonary suppuration.

Case History

This 76 year-old white man entered Mount Carmel Hospital in February of 1959 with the chief complaint of intermittent hemoptysis of 12 months' duration. The first episode was minimal in severity, but one month before admission he coughed over a pint of blood during a two-day period. There had been no hoarseness or arthralgia. His past history was noncontributory. He had worked as a carpenter for 27 years, but had been retired for two years. There had been no weight loss noted over the past months or years. Cough, productive of yellow-white sputum began one and one-half years previously.

Physical examination showed essentially normal findings. Keratotic lesions were present on the face. No lymphadenopathy was found. Breath sounds were decreased over the entire chest area. No cardiac murmur was heard. Routine laboratory tests were within limits of normal. He could climb a flight of stairs without becoming too short of breath. Roentgenograms showed a peripheral lobulated mass in the base of the right lower lobe, in close continuity to the diaphragm. This resembled a solitary lesion and the diagnosis of bronchogenic carcinoma was entertained. Bronchography delineated a bronchial block of the anterior and medial basal segments with an irregularity of the proximal lobar segmental bronchus (Fig. 1). Bronchoscopy showed suggestion of a tumor, but the biopsy obtained was not diagnostic.

With the pre-operative diagnosis of peripheral bronchogenic carcinoma or granulomatous lesion, exploratory thoracotomy was carried out on March 3, 1959. The area of destroyed lung involved at least the anterior and medial basal segments, and no characteristic tumor tissue was felt for peripheral biopsy. Right lower lobectomy was carried out, and the tumor was visualized upon examination of the resected specimen. Due to the location and polypoid nature of the lesion and because of his age and moderate pulmonary disability, a more radical procedure was not warranted. His post-operative course was uneventful, and he was discharged ten days later. He has survived over two and one-half years without evidence of recurrence or metastases.

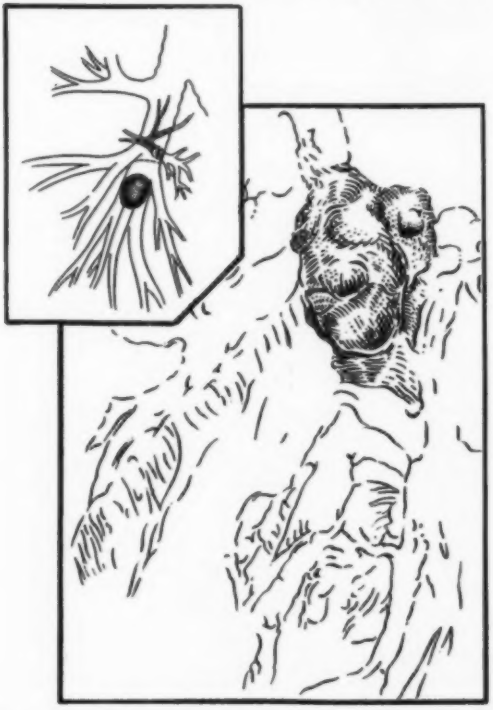

FIGURE 2b: Diagramatic outline of tumor with location in bronchus.

Gross and Microscopic Study

Gross: The specimen consisted of a resected right lower lobe of lung (Fig. 2). Upon opening the bronchi, a pedunculated solid tumor nodule was found, attached to the main stem bronchus at a point about 1 cm. from the line of resection. The tumor nodule itself measured 18 mm. in its greatest dimension. It rather effectively occluded most of the bronchi supplying the lower lobe. These were tremendously dilated and in some points they were at least 2 cm. in diameter. The lumen was filled with a thick greyish mucoid material. The lung tissue distal to the tumor was somewhat atelectatic but otherwise not remarkable. The surface of the tumor nodule was relatively smooth. It had a pink-tan color corresponding to that of the bronchial mucosa. On section, in addition to the mass of tumor lying within the lumen, there was evidence of extension of tumor through the wall of the bronchus for a distance of 5 to 6 mm.

Microscopic: Sections showed a tumor apparently arising in the wall of the bronchus. It was circumscribed, but not entirely encapsulated. In one area it seemed to extend through a cartilage of the bronchus and in this local area it was invasive. It was composed of two types of cells with some intermediate stages (Fig. 3). There were well-defined mucus-secreting columnar epithelial cells in acini. There were solid masses of prickle cells such as are found in stratified squamous epithelium. The tumor appeared to arise from the glands in the wall of the bronchus. There was prominent intimal thickening of the wall of one artery caught in a section. These findings are reasonably characteristic of a tumor which occurs in salivary glands and at the base of the tongue.

Diagnosis: Muco-epidermoid tumor.

Discussion

Recent studies of patients treated either conservatively or with pulmonary resection for cylindroid adenoma (adenoid cystic carcinoma) of the bronchus have suggested the advisability of separating into a distinct group those rare tumors showing both

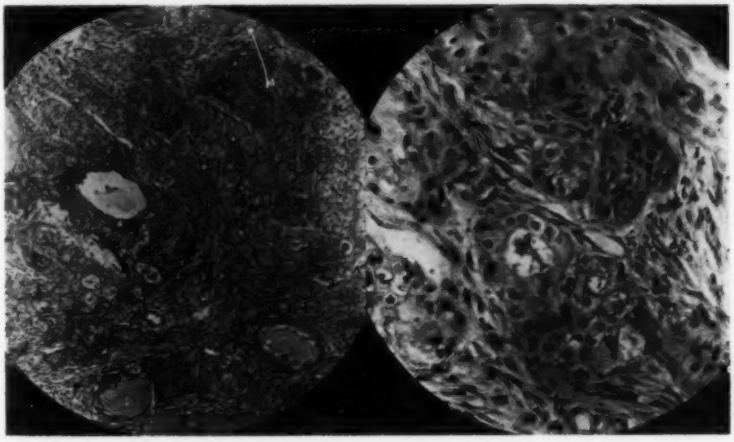

FIGURE 3a FIGURE 3b

FIGURE 3a: Low power magnification showing almost equal amounts of mucous producing cells and epithelial elements. FIGURE 3b: High power view of the lighter cytoplasm of the mucous-producing cells and the darker cytoplasm of the epithelial cells.

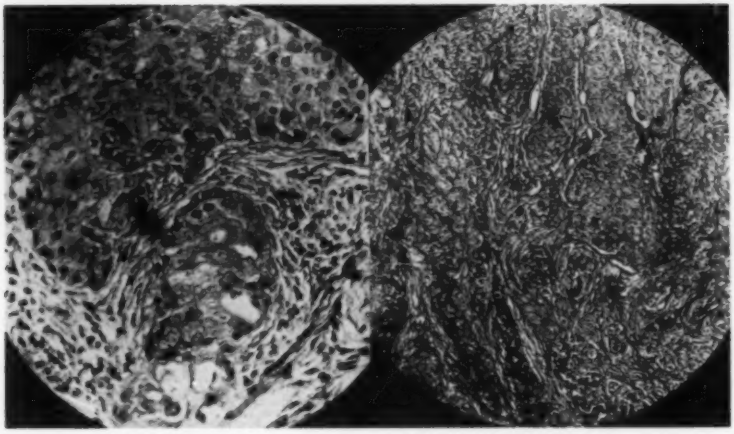

FIGURE 3c FIGURE 3d

FIGURE 3c: High power view of the lighter cytoplasm of the mucous producing cells and the darker cytoplasm of the epithelial cells. FIGURE 3d: Low power field of section stained with the periodic acid-Schiff (PAS) reaction of McManus for staining of mucin.

squamous differentiation and mucus production. These have been termed muco-epidermoid tumors. Clinically, they have failed to show local or distant metastases and produce symptoms by bronchial block with distal pulmonary suppuration. Microscopically, they are characterized by the presence of almost equal amounts of mucous cells and squamous epithelium. Involvement of the cartilage or neuro-vascular structures is minimal or nonexistent. Pulmonary resection appears to have produced a permanent cure in the small number of patients who have undergone this type of treatment.

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Two Unrelated Teratomata

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The mediastinum has now been established as a fairly common site for the occurrence of teratomata. From our experience of 90 mediastinal tumors, 10 per cent proved to be cystic teratomata at operation. This is similar to the incidence quoted in the literature.[5] The reported incidence, however, of cystic teratomata, occurring within the pericardium is rare. Until 1960, Adler *et al.* had reported ten of these cases, nine taken from the literature and one of his own.

Case Report: We observed the presence of two cystic teratomata in one patient. These tumors, one in the anterior mediastinum and the other in the pericardial cavity, showed no evidence of intercommunication, each being independent entities. To our knowledge, no similar finding has ever been reported.

The patient, R. N., a man, aged 28, agricultural laborer and father of four children, presented at the Rambam Hospital, Haifa. He complained of severe abdominal pains and fever over the past five days. The pains were sudden in onset, which occurred while he was at work and were accompanied by an acute attack of sweating. The temperature had varied around 39°C. during the five days prior to admission. He had undergone medical examination for army service one year before and was found to be completely healthy.

He was in good physical condition, but dyspneic and his blood pressure was 100/70. The pulse was full and rapid, demonstrating no irregularity of rhythm. Auscultation of the lungs revealed no abnormality. The heart sounds were forceful. No murmur was present. No hepato-jugular reflux was demonstrated. The liver edge was palpated five finger breaths below the costal margin.

The erythrocyte sedimentation rate was 23/41 mm. in two hours, hemoglobin 13.5 grams per cent, leucocytes 20,000/cmm. with shift to the left, thrombocytes 188,000/cmm., Kahn test negative, and the electrocardiogram demonstrated low voltage pattern with elevation of the ST segment in all leads. A small Q wave appeared in the second and third leads and in aVF. The venous pressure was 200 mm. of water. X-ray examination of the chest: the heart showed a marked enlargement in both directions and polycyclic shadow, the size of a small orange, was observed in the mediastinum just above the heart. Fine calcification was apparent in the walls of this shadow (Figs. 1,2).

FIGURE 1: Anteroposterior view.

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FIGURE 2: Lateral view.

The day after admission the patient developed a clinical picture of cardiac tamponade. On aspiration of the pericardium, thick pus was removed. This relieved the patient. The aspiration was repeated daily for ten days and on each occasion, 200 to 300 cc. of purulent fluid was withdrawn. This did not change in form or consistentcy even after the administration of streptokinase and streptodornase (Varidase). Bacterial cultures, including Koch's, were negative and neither amebae nor hydatid hooklets were demonstrated. Air insufflation of the pericardial cavity revealed no connection between the pericardial cavity and the radiologically demonstrated anterior mediastinal tumor. Weinberg, Casoni and Mantoux tests were negative, as were blood cultures.

His general condition improved, although a high fever persisted in spite of the administration of broad-spectrum antibiotics and on an empirical basis of emetine and chloroquine (Aralen). Since there was no improvement in the purulent process of the pericardium, and, as no diagnosis as to the tumor or its part in the clinical picture had been possible, he was transferred to the Thoracic Surgery Unit at Tel Hashomer Hospital.

In considering double pathology, the possibility of an amebic pericarditis secondary to a ruptured amebic abscess of the liver was discarded as the color of the pus was not typical, no amebae were isolated from the aspiration and there was no response to emetine. The presence of echinococcal infection of the pericardium and mediastinum was disproved by: (a) negative complement fixation and Casoni tests; (b) absence of eosinophilia; and (c) the presence of calcification.

Tuberculosis is a well known cause of purulent pericarditis. In this case it was not regarded as probable because of the absence of Koch's bacillus in the pus and the repeatedly negative Mantoux test. In addition, although the x-ray shadow could simulate the presence of tuberculosis, to our knowledge tuberculoma of the anterior mediastinum has never been described.[4] We could not exclude the possibility of malignancy producing this picture. Topographically the tumor would be situated suitably to involve the pericardium and result in a possible purulent pericarditis.

With the numerous pericardial aspirations, his condition had improved and he was

able to withstand operation. This was performed with removal of the tumor and also by performing pericardiectomy to prevent the future occurrence of constrictive pericarditis.

Left thoracotomy revealed clear straw-colored fluid in the pleural cavity. A cystic tumor, the size of a fist, was observed in the anterior mediastinum. At its superior pole, the tumor continued as a narrow pedicle which projected to the right of the sternum. The lower pole of the tumor displaced the heart inferiorly. To facilitate removal, the tumor was opened and found to contain whitish fluid, gelatinous material, hair and a mass of red, meat-like tissue. A second cystic tumor, the size of a mandarin orange, with the same content as the first tumor, was observed within the pericardial cavity. This tumor was found to be adherent to both left atrium and left ventricle. No connection could be demonstrated between these two tumors. The mediastinal mass and the mass in the pericardium were then removed and the anterior portion of the pericardial sac was excised.

The postoperative course was without incident, and the patient was discharged after 17 days. On subsequent follow-up examination two years after the operation, he was in good physical condition and actively engaged in hard physical labor.

FIGURE 3: Postoperative chest x-ray view.

Pathologic examination of the cystic tumor of the mediastinum revealed areas of fibrotic and gelatinous tissue. The wall of the tumor was lined by a flat epithelium showing features of cornification. Deep within the epithelium lining were nests of skin tissue, sebaceous and sweat glands. The ducts of these glands were lined with flat and cylindrical epithelial cells, simulating epithelium of the respiratory tracts. Calcification was present in various parts of the tumor.

Histologic examination of the tumor from the pericardial cavity revealed that the lining of the cyst had been destroyed by a chronic infective process which was nonspecific. This lining had then been replaced by granulation tissue. In one area, yellow cornified material was found. Foreign body giant cells, foamy cells and cholesterol crystals were observed interspersed among the other contents. No evidence of malignancy was demonstrated.

Comments: The sudden, abrupt appearance of the clinical picture remains to be explained. Cystic teratomata are by definition of congenital origin and thus the sudden onset of acute infection within the cyst at the age of 28 is indeed strange. Rusby[3] has suggested that infection can be spread from the lung to the cyst by contiguity or by transport of organisms from outlying infective foci via the blood stream. Furthermore, he continues "the advent of infection within the cyst is frequently so dramatic in onset and so grave in outcome that it may be reckoned one of the most dreaded complications of an apparently benign symptomless dermoid tumor!"

The pathologic diagnosis of an anterior mediastinal tumor in our case was established by the demonstration of the presence of all three germinal layers. The diagnosis of the pericardial tumor, however, proved more difficult, as the cyst lining had been totally destroyed by the chronic infective process. As the contents proved to be identical with that found in the anterior mediastinal tumor, a diagnosis of cystic teratoma of the pericardium was justified.

Of the ten cases of intrapericardial cystic teratomata discussed by Adler *et al.*,[6] seven were infants, two of which were premature. The diagnosis was established either at operation (four cases) or at necropsy.

To our knowledge, ours is the first case described of two unrelated cystic teratomata of the mediastinum, occurring in the same patient.

ACKNOWLEDGMENT: We wish to acknowledge help received from D. Barzilai, M.D., and Ilana Tatarsky, M.D., Department of Medicine, Rambam, Haifa.

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COMPARATIVE VALUE OF ROENTGENOLOGIC FINDINGS IN PULMONARY EMPHYSEMA

The purpose of this work was to assess the roentgenologic findings in chronic emphysema: decrease of the difference in the pulmonary fields transparency during inspiration and expiration (Y. N. Sokolov), diminution of the difference in the size of the retracardial space during inspiration and expiration (Kalinovsky) and absence of changes in the caliber of pulmonary vessels during the tests of Valsalva and Muller (Rigler). According to the author, of greatest value are the tests of Sokolov and Kalinovsky, positive in 80 per cent of cases and suitable for assessing the severity of emphysema. Kalinovsky's test is of special value in ambulatory patients, inasmuch as it does not require roentgenography.

Brener, D. M.: "On the Comparative Value of Roentgenologic Symptoms in Pulmonary Emphysema." *Clin. Med. (USSR)*, 39:74, 1961.

CHRONIC BRONCHITIS IN AFRICAN MINERS AND NON-MINERS IN NORTHERN RHODESIA

Chronic bronchitis is a disabling condition which, in several countries, has superseded pulmonary tuberculosis in importance as a disease of the respiratory system. The Ministry of Pensions and National Insurance report that in the year 1955-56, almost 27,000,000 working days were lost as a result of bronchitis in the "insured" population of Great Britain.

At this Bureau, 35,000 African mine workers from the six copper mines of Northern Rhodesia are clinically and radiologically examined each year. Over the past 15 years, 100,000 individual African mine workers have been so examined and it has been our observation that the incidence of chronic bronchitis in this population is very low. All are exposed to silica dust, the maximum permissible limit of which, in the range between 0.4 and 7 microns, is 350 particles per cc. The free silica content of this fine atmospheric dust as determined by the x-ray diffraction method using the Geiger counter technique varies in the six mines from 19 to 43 per cent.

In this study, the low incidence of chronic bronchitis found in 3536 African copper miners and 1,118 non-miners in Northern Rhodesia is recorded. Histologic examination of the lungs of 675 deceased African miners also revealed a low incidence. There was little evidence that dust was an important etiologic factor in the development of chronic bronchitis, it is considered that there are many etiologic factors in the development of the disease, of which smoking and atmospheric pollution are probably important.

Paul, R.: "Chronic Bronchitis in African Miners and Non-miners in Northern Rhodesia," *Brit. J. Dis. Chest*, LV:30, 1961.

Chronic Interstitial Pneumonitis of the Azygos Lobe

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Big Spring, Texas

In several large series of cases reported, the azygos lobe was found to occur in 0.1 to 4 per cent of all chest x-ray films.[1] However, diseases of the azygos lobe are rarely seen, and it is for this reason this report is presented. The following is a case report of nonspecific chronic interstitial pneumonitis of an azygos lobe which was surgically removed.

Case Report

This 48 year-old white man was admitted to the medical service of the Big Spring Veterans Administration Hospital with a three-week history of chills, fever, and increased weakness.

The history revealed a 20-pound weight loss during the past three months. He also stated that about ten years ago he was in another hospital for pneumonia and was discharged after eight days' treatment. During the past ten years, his health has been excellent and he has worked regularly as a carpenter.

On examination, the rectal temperature was 102.6°F., blood pressure 130/62, pulse 120. He appeared acutely and chronically ill, with evidence of recent weight loss. There were bilateral enlargement and tenderness of the cervical lymph nodes. Healing herpes labialis and severe pyorrhea were present. The chest showed symmetrical, normal expansion. There was dullness with decreased breath sounds over the right upper lung field. Rales were not heard. The remainder of the physical and neurologic examination revealed no other abnormality. The hemoglobin was 11.3 grams, red blood cell count 3.2 million, white blood cell count 10,500, with 70 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes, 6 per cent monocytes, and 1 eosinophil. Urinalysis and urine culture were negative. Three smears were negative for acid-fast

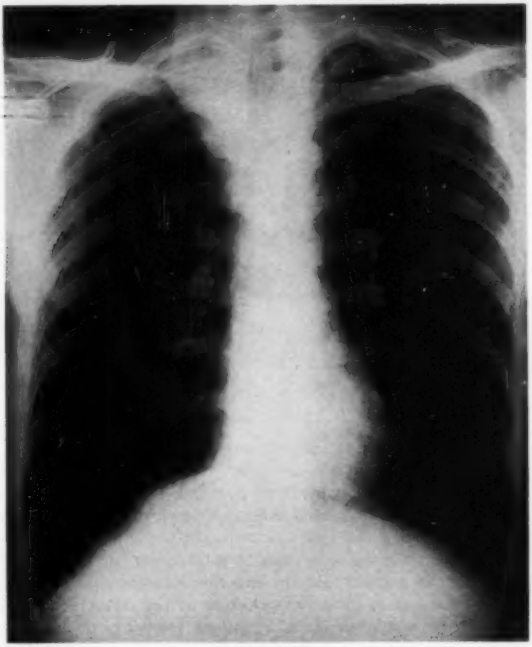

FIGURE 1

*Chief, Medical Service, Veterans Administration Hospital.

bacilli. Sputum culture demonstrated a heavy growth of non-hemolytic Staphylococcus albus, which was coagulase negative. The serologic test for syphilis was negative as were agglutination tests for typhoid, paratyphoid, tularemia, and brucellosis. Proteus OX-19, Paul-Bunnell test for infectious mononucleosis, and cold agglutinin test were also negative. The chest x-ray film demonstrated a mass in the right superior mediastinum. It was felt that this probably represented consolidation in an azygos lobe (Fig. 1). Stratigrams revealed a similar finding. Skin tests for tuberculosis, coccidioidomycosis, blastomycosis, and histoplasmosis were negative.

He was treated with penicillin, streptomycin, and tetracycline. He remained febrile for about ten days. Because of the possibility of malignancy, exploratory thoracotomy was performed. A dense adhesive pleuritis of the entire chest space was found. It was felt that the disease was in an azygos lobe, which was clearly identified. Because of the possibility that this could be a carcinoma and for technical reasons, the right upper lobe was removed along with the azygos lobe. The postoperative course was uneventful.

PATHOLOGY REPORT: *Gross:* The azygos lobe showed induration and scarring with diffuse anthracosis. *Microscopic:* Granulomatous inflammation characterized by chronic fibrotic pleurisy and chronic fibrotic pneumonitis. Some alveolar spaces showed fluid or a pink staining exudate, but others were occluded with scar tissue. The pleural surfaces were thick, fibrotic, and lightly infiltrated with lymphocytes. The alveolar cells were quite prominent and hyperplastic. Few areas revealed purulent inflammation in the form of small abscesses in which a few giant cells were found. These were not Langhans' giant cells. No caseation or frank tubercles were seen. Anthracosis was present in large deposits. There was no unusual arteriosclerosis of the pulmonary vessels. Special stains revealed no fungi. Many of the macrophages present in the alveolar spaces contained granules which possibly were cholesterol deposits. This type of reaction has been described as chronic pneumonia, "cholesterol type," with interstitial fibrosis. There was no evidence of malignancy. *Diagnosis:* Chronic interstitial pneumonitis, azygos lobe.

In 1956, a case of pulmonary tuberculosis involving the azygos lobe alone was presented and the authors believed that theirs was the first case so reported.[3] Pneumonia of an azygos lobe was described in a boy following measles.[1] An unusual case was also noted where the patient had blastomycosis involving the entire right upper lobe, but sparing the azygos lobe.[4] An interesting case was described of a man of 70 years with rheumatic heart disease who at necropsy was found to have hydrothorax with the accessory lobe floating in the fluid. The pedicle of the lobe was twisted through two and one-half complete turns.[2]

The case here described is probably the first reported of nonspecific chronic interstitial pneumonitis involving only the azygos lobe.

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VENTRICULAR TACHYCARDIA

The effect on cardiac rhythm of the intravenous administration of metaraminol (Aramine) during cyclopropane anesthesia in dogs has been investigated. Injection of a standard dose of epinephrine, sufficient to produce ventricular tachycardia, was used as a control. Metaraminol in a dose of 0.1 mg./kg. of body weight produced multifocal ventricular tachycardia in six of the ten dogs anesthetized with cyclopropane. When the dose was increased to 0.2 mg./kg. of body weight, a dose closely approximating an equal vasopressor dose of epinephrine, eight of the ten dogs developed this arrhythmia. The controlled study and the experiments simulating clinical conditions would indicate that the use of metaraminol is contraindicated during cyclopropane anesthesia. Further, cyclopropane should not be administered to a patient receiving, or recently having received metaraminol.

Siebecker, K. L., Bamforth, B. J., Kraemer, R., and Orth, O. S.: "Ventricular Tachycardia Produced by Metaraminol during Cyclopropane Anesthesia in Dogs," *Anesthesiology,* 22:555, 1961.

ROENTGENOGRAM OF THE MONTH

Edited by Benjamin Felson, M.D.

WILLIAM W. JOULE, M.D.*
Louisville, Kentucky

Clinical Information

This 27 year-old white woman entered the hospital in August, 1960 with a three-week history of numerous episodes of epistaxis. She was in good health until four months ago when she complained of being weak and "washed-out." This malaise became so severe that she was bed-ridden during the last two months of her illness. She had a non-productive cough, and appeared weak and pale. Her hemoglobin was 2.8 grams and there was gross blood in her urine. The admission chest film was normal. Bone marrow from the sternum and vertebrae showed markedly decreased erythropoiesis and myelopoiesis compatible with aplastic anemia. This was the clinical impression. A chest film taken 13 days after the normal admission film and two days before she expired is presented below.

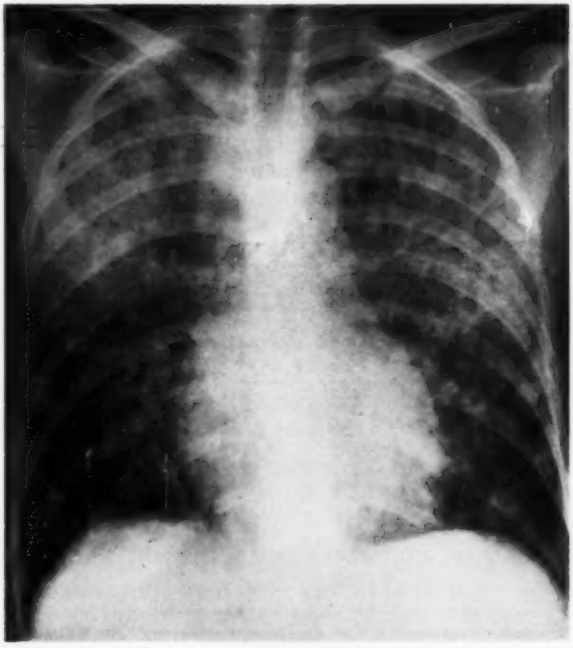

FIGURE 1

*From the University of Louisville School of Medicine.

Answer: PULMONARY AND CARDIAC ASPERGILLOSIS

In man, *Aspergillus fumigatus* and *Aspergillus niger* can be pathogenic. Birds are the most common carriers, pigeons and penguins being especially heavily infected. Stockyard, slaughter house and grain workers, farmers and pigeon feeders are most commonly primarily infected. Infection is usually bronchogenous rather than hematogenous. Tissue damage following bronchiectasis, tuberculosis, carcinoma, pulmonary infarction, and generalized diseases such as diabetes mellitus and aplastic anemia, aids in the growth and spread of the fungus. Pulmonary aspergillosis without previous lung damage is rare. When grown in culture media, conical sporangiosphores are formed at the end of clubshaped hyphae; however, when growing in tissues, as a rule, only hyphae are seen.

Multiplication and spread of the fungus follows no particular anatomic pattern in the lung. Radiologically, the disease may be found as segmental pneumonia which eventually resolves or in which central cavities may form. More commonly, as in this case, it is seen as a bilateral nodular infiltrate. Miliary-sized nodules favor the diagnosis of tuberculosis rather than aspergillosis. Hilar adenopathy may be present. This disease can heal with the formation of fibrosis and calcification. If the patient becomes sensitized to the fungus, asthma-like symptoms may develop.

A third type of pulmonary aspergillosis sometimes occurs if the fungus erodes through the wall of a bronchus. A gradually expanding cavity is produced in which the multiplying hyphae mass together in a ball. Radiologically, this often produces a crescent-shaped air shadow which will change its relative position when the patient's position is changed due to displacement of the fungus ball within the cavity.

The aspergillosis infection rarely involves adjacent structures. In this patient, a 1 x 2 cm. mycetoma was found in the interventricular septum of the heart. This growth represented a direct extension from the pulmonary infection.

The Committee on Chest Roentgenology welcomes comments. We would also be pleased to receive x-ray films of exceptional interest with a brief history. Please submit material to: Benjamin Felson, M.D., Department of Radiology, Cincinnati General Hospital, Cincinnati, Ohio.

LUNG CANCER AMONG INDIANS OF THE SOUTHWESTERN UNITED STATES

A striking absence of lung cancer was found among Indians of the southwestern United States in a seven-year hospital study. It is not known whether hereditary or environmental factors are related to this deficit. However, minimal exposure to industrial fumes and infrequent use of cigarettes among the Indian population may be noteworthy findings.

Sievers, M. L., and Cohen, S. L.: "Lung Cancer Among Indians of the Southwestern United States," *Ann. Int. Med.*, 54:912, 1961.

SECTION ON CARDIOVASCULAR DISEASES

The Effect of Exercise upon the Mean Systolic Left Ventricular-Brachial Artery Gradient in Aortic Stenosis*

PHILIP SAMET, M.D., F.C.C.P., WILLIAM H. BERNSTEIN, M.D., and ROBERT S. LITWAK, M.D., F.C.C.P.
Miami Beach, Florida

The purpose of this study is to determine the effects of variations in cardiac output upon the mean systolic left ventricular-brachial artery gradient in patients with aortic stenosis.

The magnitude of this gradient varies with valve size, flow across the valve and possibly heart rate. The effect of these parameters has been investigated in patients with mitral stenosis.[1,2] Since exertional dyspnea, angina and syncope are common in physiologically significant aortic stenosis, determination of the exercise aortic gradient is of considerable interest in evaluation of the mechanism of these symptoms. In principle, exercise gradient changes may result from alterations in left ventricular systolic pressure, brachial artery systolic pressure, or both factors.

TABLE 1—PHISICAL CHARACTERISTICS AND DIAGNOSES IN FOUR CASES WITH AORTIC STENOSIS

Patient	Sex	Age (Yr.)	B.S.A. ($M.^2$)	Diagnosis
G. And.	M	50	1.86	Rh. H.D. E.H. A.S. N.S.R. II C.
G. Woo.	M	37	1.81	Rh. H.D. E.H. A.S. N.S.R. III C.
G. Smi.	M	16	1.78	Cong. H.D. E.H. Valvular A.S. Minimal A.I. N.S.R. II C.
S. Ber.	F	53	1.41	Rh. H.D. E.H. M.S. A.S. A.F. II C.

TABLE 2—CARDIAC OUTPUT DATA DURING COMBINED HEART CATHETERIZATION

Patient	Vent. Rate (/Min.)		Cardiac Index (L./Min./$M.^2$)	Stroke Vol. (ml.)	Oxygen Consumption (Ml./Min./$M.^2$)	R^2	A-V Dif. (Vol. %)	SA_{O_2} per cent
G. And.	R[a]	68	2.94	80	153	.78	5.2	94
	E[a]	89	3.82	80	336	.99	8.8	96
G. Woo.	R	84	2.91	63	162	.87	5.6	93
	E	101	4.18	75	293	.90	5.5	93
G. Smi.	R	68	3.93	103	151	.87	3.8	94
	E	80	4.16	93	266	.88	6.4	96
S. Ber.	R[a]	67	2.20	48	100	.97	4.6	98
	E[a]	88	2.91	47	222	1.02	7.6	97

a. Obtained during right heart catheterization only.

*From the Cardio-Pulmonary Laboratory and the Department of Medicine, Mount Sinai Hospital, Miami Beach, and the Departments of Medicine and Surgery, University of Miami School of Medicine, Coral Gables.

Methods and Materials

The physical characteristics and diagnoses in the four patients are given below (Table 1). Right heart catheterization, brachial artery cannulation and posterior percutaneous left atrial puncture were performed as previously described.[2] Data were obtained at rest and during exercise in the course of combined right and left heart catheterization. Cardiac output was determined by the Fick principle.

The left ventricular-brachial artery gradient was calculated via planimetric integration of the systolic pressure difference between the left

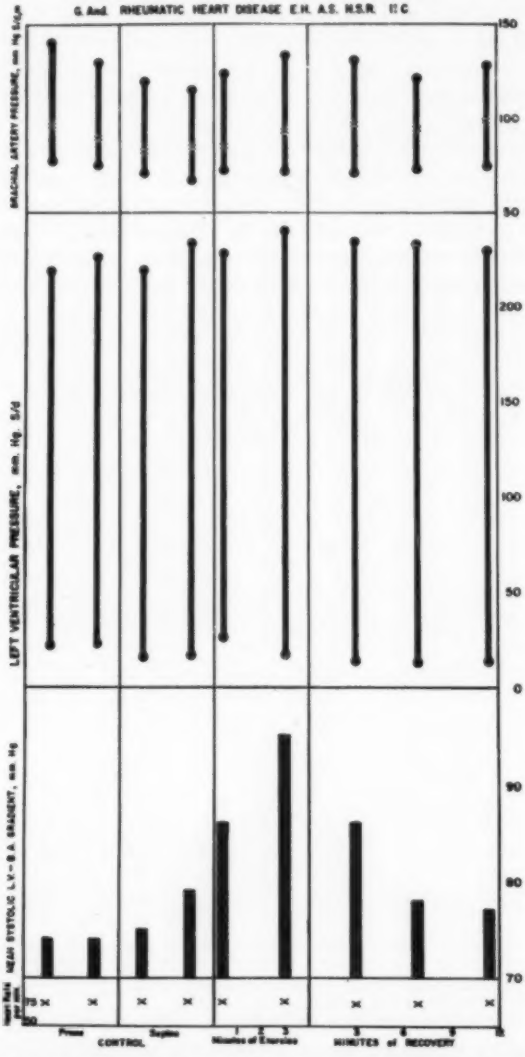

FIGURE 1: Left ventricular and brachial artery pressures and systolic gradients in G. And. The gradient increases about 15 mm. Hg during exercise.

ventricular and brachial artery pressure curves, recorded from the same base-line at identical stain gauge sensitivities. At least six beats were studied for each gradient determination. Theoretically, determination of the left ventricular-aortic mean systolic gradient is preferable. In actual practice, however, the ventricular-brachial artery systolic gradient is only about 10 per cent less than the simultaneously determined ventricular-aortic systolic gradient.

Results

The cardiac output and pressure data are presented in Table 2, and Figs. 1 to 4.

The control left ventricular-brachial artery mean systolic gradients in G. And. ranged from 74 to 79 mm. Hg. During exercise the gradient increased to 95 mm. Hg and fell to 77 during recovery (Fig. 1). Cardiac output data during right heart catheterization alone earlier during the

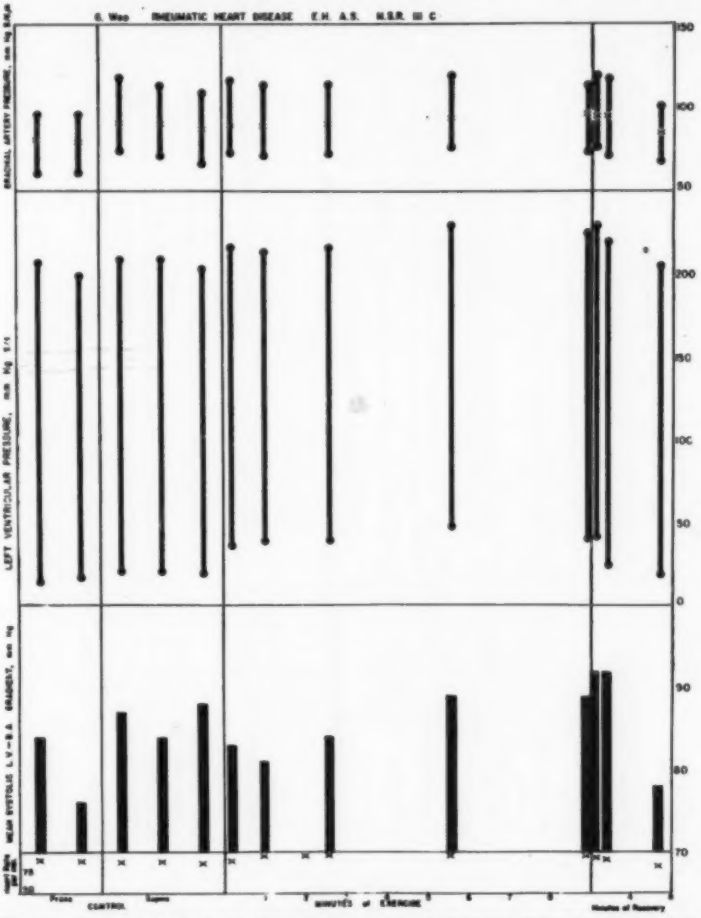

FIGURE 2: Similar data in G. Woo. The gradient changes during exercise are minimal. Left ventricular end-diastolic pressures rise sharply in the course of exercise.

same catheterization revealed an exercise factor of 480. That is, the cardiac output during exercise increased 480 ml. for each 100 ml. increase in oxygen consumption. The normal range is 600-1000 ml. per 100 ml. increment in oxygen utilization. Systolic left ventricular pressure rose from control levels of 220 mm. Hg to exercise levels of about 245 mm. Hg. Left ventricular end-diastolic pressure was slightly elevated at rest and rose to more abnormal levels during exercise.

The control gradients in G. Woo. ranged from 76 to 88 mm. Hg (Fig. 2). There was no change during exercise. During early recovery the gradient was 92 mm. Hg. The exercise factor during combined right and left heart catheterization was 970 ml. Left ventricular systolic pressure rose slightly during exercise; left ventricular end-diastolic pressure rose markedly during exercise to 46 mm. Hg. Pulmonary edema did not develop during exercise despite this gross elevation in left ventricular end-diastolic pressure.

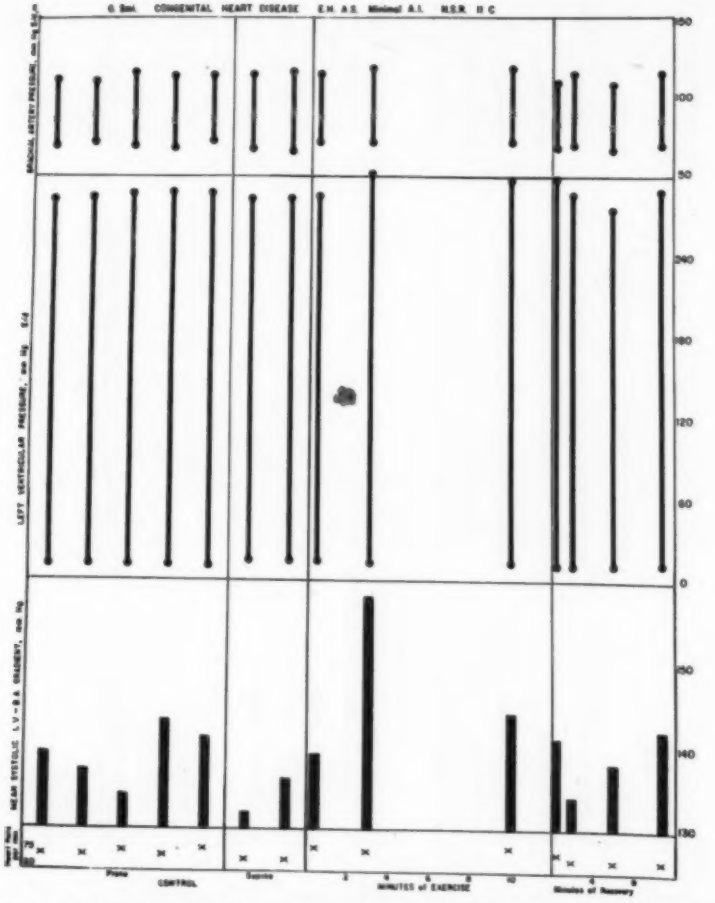
G. Smi. CONGENITAL HEART DISEASE E.H. A.S. Minimal A.I. N.S.R. II C
BRACHIAL ARTERY PRESSURE, mm Hg
LEFT VENTRICULAR PRESSURE, mm Hg
MEAN SYSTOLIC L.V.—B.A. GRADIENT, mm Hg
Supine
CONTROL
MINUTES of EXERCISE
Minutes of Recovery

FIGURE 3: Left heart catheterization values in G. Smi. A mild increase in left ventricular-brachial artery systolic gradient is noted during exercise.

The control gradients in G. Smi. (Fig. 3) ranged from 134 to 143 mm. Hg. During exercise the gradient rose to 158 mm. Hg, but returned to control levels during recovery. Left ventricular systolic pressures were about 285 at rest and rose slightly to 300 during exercise. No change was noted in left ventricular end-diastolic pressure during exercise. The exercise factor totaled 200 ml.

Severe aortic stenosis was present in the first three subjects. In the fourth, S. Ber. (Fig. 4) the predominant lesion was mitral stenosis; the aortic stenotic lesion was of little physiologic import The control aortic

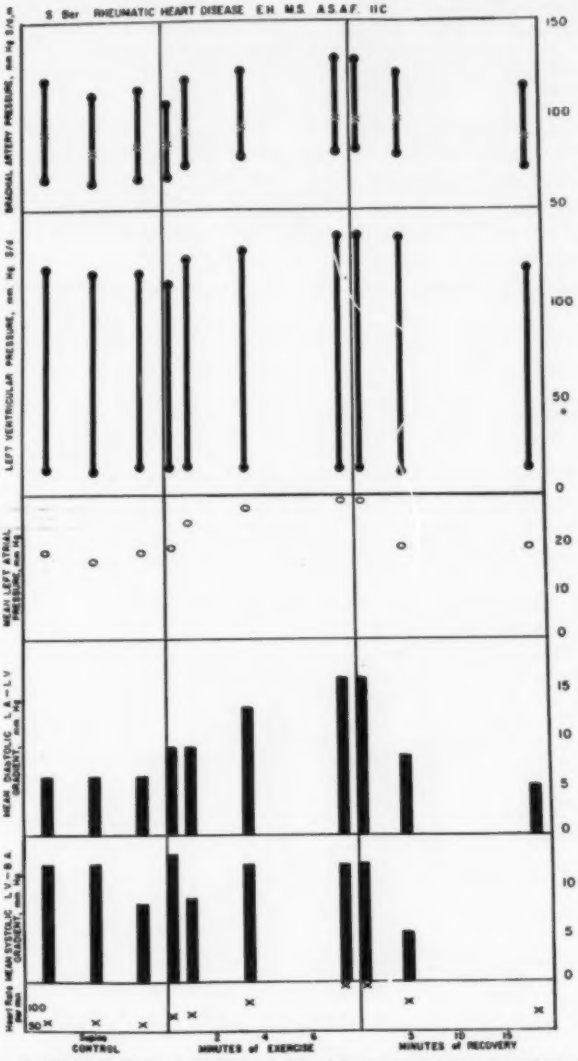

FIGURE 4: Catheterization data in S. Ber. The percentage exercise increment in left ventricular-brachial artery systolic gradient is far less than that of the diastolic left atrial-left ventricular gradient.

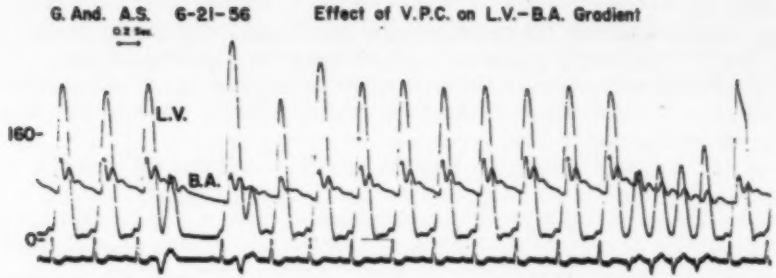

FIGURE 5: Variation of left ventricular-brachial artery systolic gradient during and after ventricular premature beats in G. And. Transient post-extrasystole ventricular pulsus alternans is to be noted.

systolic gradients ranged from 8 to 12 mm. Hg. No significant increase was noted during exercise. In contrast, the mitral diastolic gradient more than doubled during exercise. Left ventricular systolic pressure rose slightly during exercise; left ventricular end-diastolic pressure was unchanged. Left atrial mean pressure rose significantly during exercise. The exercise factor, during the preceding right heart catheterization alone, was slightly subnormal, 580 ml.

Discussion

The magnitude of the mean systolic left ventricular-brachial artery gradient may vary under the influence of a number of factors. Increase in blood flow during exercise had surprisingly little effect upon the magnitude of the systolic aortic gradient. This observation was noted even when the increase in output and stroke volume during exercise were significant, as in G. Woo. These data are in marked contrast to the large exercise increase in mean diastolic mitral gradient previously noted in patients with mitral stenosis even when the exercise cardiac output and stroke volume increases were small.[1]

Other studies have, however, indicated that alterations in heart rate and or left ventricular filling will affect the aortic systolic gradient. For example in Fig. 5, the aortic systolic gradient is minimal or absent in the course of ventricular premature beats. The post-premature beat gradient is, on the other hand, considerably larger

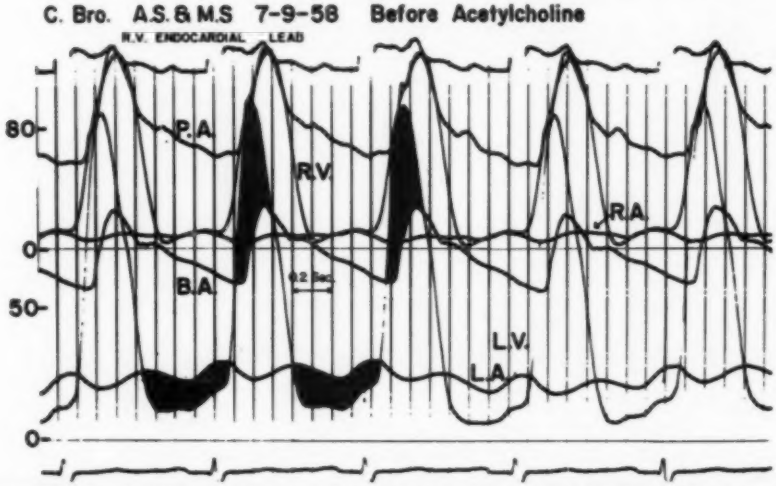

FIGURE 6: Semilunar valve systolic gradient prior to acetylcholine infusion in a patient with combined aortic and mitral stenosis.

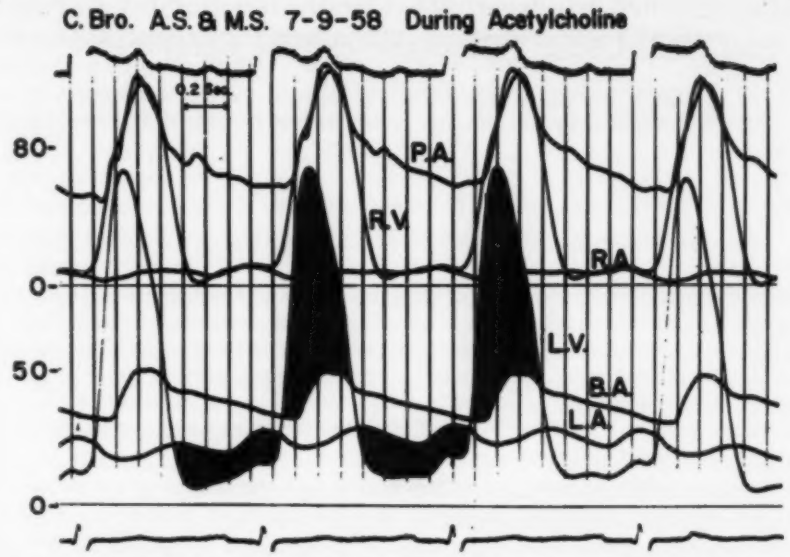

FIGURE 7: The increase in systolic gradient consequent to acetylcholine infusion and systemic arterial hypotension is readily noted in the same patient as in Fig. 6.

than the control gradient. Beat to beat variation in the aortic systolic gradient may be noted during atrial fibrillation.

Left ventricular pulsus alternans also results in alteration of the magnitude of the aortic systolic gradient. Variations in systemic arterial pressure result in changes in aortic systolic gradient (Figs. 6 and 7). Right and left heart pressures are recorded simultaneously in a patient with aortic and mitral stenosis. The moderate aortic gradient noted prior to intracardiac acetylcholine infusion increased sharply during acetylcholine infusion with the development of systemic arterial hypotension and the presumed decrease in peripheral vascular resistance.

The explanation for the minimal rise of the aortic systolic gradient during exercise despite sizeable elevations of cardiac output and oxygen consumption remains uncertain, but the data are in sharp contrast to the behavior of the mitral diastolic gradient under similar exercise conditions.

SUMMARY

Measurements of the mean systolic left ventricular-brachial artery gradient and cardiac output at rest and during exercise in four subjects with aortic stenosis were made in the course of combined right and left heart catheterization. Only minimal elevations were noted in the aortic systolic gradient during exercise despite significant flow increases in three of the four patients.

RESUMEN

La medición el medio gradiente sistolico ventricular izquierdo-arteria braquial y el rendimiento cardiaco durante el ejercicio y el repose en cuatro sujetos con estenosis aórtica se hizo en el curso de la cateterización cardiaca combinada izquierda y derecha. Solo elovaciones mínimas se notaron en el gradiente sistolico durante el ejercicio a pesar de aumento significante del fluoj en tres de los cuatro enfermos.

ZUSAMMENFASSUNG

Es wurden Messungen des mittleren systolischen Druckgefälles zwischen linker Kammer-Brachialarterie und Schlagvolumen in Ruhe und bei Belastung an 4 Personen mit Aortenstenose vorgenommen, und zwar im Veriauf einer kombinierten Katheterisierung des rechten und linken Herzens. Es wurde bei Belastung nur ein minimaler Anstieg am systolischen Aortengradienten beobachtet während Belastung trotz beträchtlicher Zunahme der Strömungsgeschwindigkeit bei 3 von 4 Patienten.

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Maintenance of Adequate Circulation during Cardiac Standstill Using a Mechano-cardiac Compressor* **

PHILIP Y. ATTALLA, M.D., CESAR BORQUEZ VIAL, M.D., F.C.C.P., PETER V. MOULDER, M.D., F.C.C.P., and WILLIAM E. ADAMS, M.D., F.C.C.P.
Chicago, Illinois

Introduction

The recent rise in the incidence of cardiac arrest may be attributed in part to an actual increase in the frequency of this condition and in part to better recognition by anesthesiologists and surgeons of this ever present danger. In addition, the ever-increasing number of major intrathoracic and abdominal operations must be recognized as a major factor in the increased incidence of carriac arrest. Improvement in techniques today permits poor risk patients to be subjected to such surgical procedures, and many of them are afflicted by one or more of the conditions often considered to predispose to cardiac standstill.

Cardiac arrest occurs as a complication in approximately 0.1 per cent of all surgical patients.[1] Analysis of 1200 cases of cardiac arrest by Stephenson revealed that 87 per cent of cases occurred in the operating room and 13 per cent elsewhere.[2] Hypoxia, hypercarbia and neurovascular reflexes appear to predispose to cardiac standstill.

Awareness of the possibility of salvage in cases of cardiac arrest is evident in clinical reports regarding this condition. Cole reported 350 cases of cardiac arrest from the literature with recovery of 112 (32 per cent).[9] Papper reported a 44 per cent survival rate following cardiac resuscitation, and estimated that one should anticipate a 75 per cent survival if effective therapy were instituted promptly.[10]

All agree that manual cardiac massage is the treatment of choice for cardiac arrest. However, the major question concerns the length of the interval which intervenes between cardiac arrest and the initiation of effective massage. This question was answered by Stephenson in 1954 when he emphasized the importance of entering the thoracic cavity and starting the massage within four minutes.[2] In his analysis of 1200 cases he estimated that "In 94 per cent of the cases that were considered successful, the heart was massaged within four minutes while only 6 per cent survived after a delay over four minutes."

Experience has shown that there were great variations in the ability of different surgeons to obtain satisfactory pressures from manual cardiac massage. Inadequate systemic pressure, trauma to the heart, including massive contusions or rupture, acute hemorrhagic necrosis of the ventricle, and pulmonary edema have been reported as some of the complications of manual cardiac massage.[5,6,8] Fatigue of the operator commonly results from manual massage, especially if the maneuver had to be carried out for long periods of time, in which case two or more qualified persons had to be available to relieve one another.

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*From the Department of Surgery, University of Chicago.
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An additional important question arose. How long should one massage the heart? Often the surgeon is likely to be discouraged too early; however, frequently a flabby and atonic myocardium can be restored to an actively beating organ. Stephenson succeeded in resuscitating a heart to active rhythmical cardiac action after two hours of massage.[3] Hosler in 1950 successfully restored a heart after eight hours of cardiac massage. According to him, one rule of thumb is to continue to massage as long as one is convinced that artificial cerebral circulation has been adequate enough to prevent irreversible damage to the cortical cells.[13]

The next question concerns the value of drugs in cardiac arrest. Experimental investigations by Stephenson in which several medications were injected intracardially were of great value in answering this question. The injection of epinephrine or calcium chloride solution into the heart as soon as it was exposed for cardiac massage was of apparent benefit; however, many cases required only manual massage before a forceful and regular rhythm returned.[14] Procaine added to epinephrine to avoid ventricular fibrillation was discontinued because of the resulting diminution of tone to the myocardium and its questionable protection against fibrillation. The use of nikethamide (Coramine), caffeine and pentylene tetrazol (Metrazol) were also of no value in resuscitating the heart, the reason being that those drugs were primarily cerebral stimulants and would increase the metabolic demands of the already oxygen-depleted cortical cells, thereby causing further neurologic sequela or death.

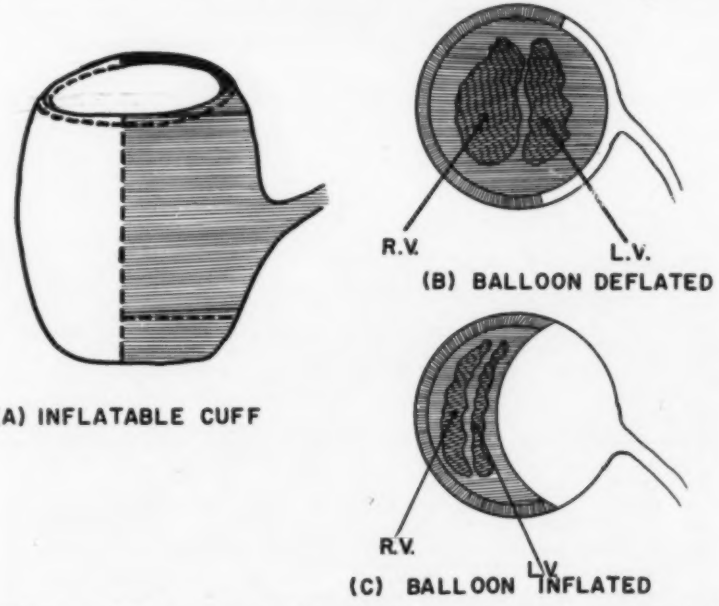

FIGURE 1: (A) The mechano-cardiac pulsator. The inflatable compartment of the cuff connected to the rubber tube through which air can be rhythmically introduced. (B) Rubber cuff deflated. (C) Rubber cuff inflated exerting localized pressure on the left ventricle; right ventricle is compressed indirectly through the pressure transmitted from the left side.

The above findings of Stephenson agree favorably with the experimental work done in this laboratory. However, it was found that the addition of 4 ml. of l-arterenol (Levophed) to 500 ml. of normal saline given through the intravenous catheter in a very slow rate, about five minutes, before the end of the massage was most helpful in increasing the tone of the cardiac muscle fibers.

Consistent with the previous discussion is the opinion that mechanical cardiac massage is the most important factor in the resuscitation of patients undergoing cardiac arrest. Consequently the problem of maintaining adequate systemic circulation during cardiac standstill by mechanical means has created great interest among research workers. Bencini in 1956 employed mechanical pneumomassage of the heart in dogs.[3] Cardiac massage was effected through rhythmical air inflation into the pericardial sac. This, however, proved to be unsatisfactory because of the resultant high venous and pulmonary artery pressure, and impaired coronary circulation plus the necessity of an intact pericardium and the time required for cannulation. These findings were substantiated in this laboratory by Jones, *et al.*[11] Vineberg in 1957 reported his experimental work on the canine heart.[4] Cardiac arrest was produced after two minutes of anoxia and the heart then was massaged for eight minutes. He used an apparatus which he described as the mechanical heart. Two rubber bags were applied over the left and right ventricles and were inflated rhythmically through air pressure. None of the dogs had any evidence of coronary, myocardial or gross epicardial damage. However,

TABLE 1—SYSTEMIC AND PULMONIC ARTERIAL PRESSURES IN 21 DOGS OVER PERIODS UP TO TWO HOURS

Serial No.	Dog No.	Date	Air Pres. mm./Hg	Systemic Pressure mm./Hg		Pulmonary Pressure mm./Hg		Duration of Massage in Min.	Status	
				S/D	Mean	S/D	Mean		At End of Procedure	Postoperative Course
1	522	12-30-59	250	85/35	40	40/20	28	20	Alive	Died 3 days—Infection
2	599	1-4-60	300	50/25	30	25/12	18	20	Alive	Sacrificed 22 days
3	820	1-8-60	200	100/60	75	32/17	20	20	Alive	Sacrificed 42 days
4	638	1-12-60	250	85/40	60	35/20	25	30	Dead	Anesthetic Death
5	925	1-14-60	275	55/30	40	22/10	15	20	Alive	Died 6 days—Infection
6	529	1-15-60	300	80/20	40	—	—	20	Alive	Died 3 days
7	628	1-19-60	200	75/45	55	30/22	27	25	Alive	Sacrificed 13 days
8	526	1-20-60	180	70/45	45	32/23	25	25	Alive	Died 5 days
9	762	1-22-60	275	75/45	50	30/20	22	60	Dead	Overdose medication
10	865	1-27-60	250	65/30	40	22/18	20	60	Alive	Sacrificed 23 days
11	747	2-1-60	200	65/40	50	30/20	25	45	Alive	Sacrificed 12 days
12	486	2-3-60	100	80/40	50	45/30	35	60	Alive	Sacrificed 10 days
13	844	2-4-60	200	90/50	65	35/20	25	60	Alive	Sacrificed 23 days
14	722	2-8-60	125	70/35	50	30/12	17	60	Alive	Sacrificed 26 days
15	748	2-12-60	200	65/40	50	30/15	20	40	Alive	Sacrificed 21 days
16	523	3-7-60	180	60/35	40	30/20	25	60	Alive	Sacrificed 10 days
17	839	3-16-60	200	65/40	50	30/20	25	60	Alive	Died 5 days
18	525	4-6-60	140	75/50	60	27/20	25	75	Alive	Sacrificed 12 days
19	520	4-27-60	100	90/50	65	35/15	20	120	Alive	Sacrificed 23 days
20	629	5-12-60	180	65/45	50	32/17	20	75	Alive	Sacrificed 12 days
21	622	5-17-60	140	65/40	50	30/12	17	45	Alive	Sacrificed 10 days

the eight-minute period is too short to prove its efficiency in conditions necessitating long periods of massage.

The following report concerns our experience with a mechano-cardiac pulsator which has been developed in this laboratory. The device was found to be capable of maintaining adequate systemic circulation during cardiac standstill for periods of at least two hours.

Experimental Method

Apparatus

The mechano-cardiac pulsator was designed to mimic the normal cardiac cycle and pressures in the different chambers of the heart, *viz*: a high systemic presure, a low pulmonary artery pressure with regular rhythmical beats of 80 per minute, with attention to the systolic-diastolic a high systemic pressure, a low pulmonary artery pressure with regular relation. The apparatus consists of a latex rubber bag, shaped like a heart, with upper and lower openings. It is made of two layers (a) an outer firm and less distensible layer, and (b) an inner more elastic one. The two layers are sewn and glued in such a way that one-half forms a blind compartment that does not distend on inflation and lies over the right ventricle, while the other one-half of the circumference forms the inflatable compressible compartment and lies over the left ventricle. The chamber is connected with a rubber tube through which air is rhythmically introduced and the compartment thus inflated (See Fig. 1).

From the previous description it is apparent that the pressure is applied selectively over the left ventricle while the right ventricle is affected indirectly through the transmitted pressure from the left side. Air or oxygen can be used and is received through a pressure outlet. The bag

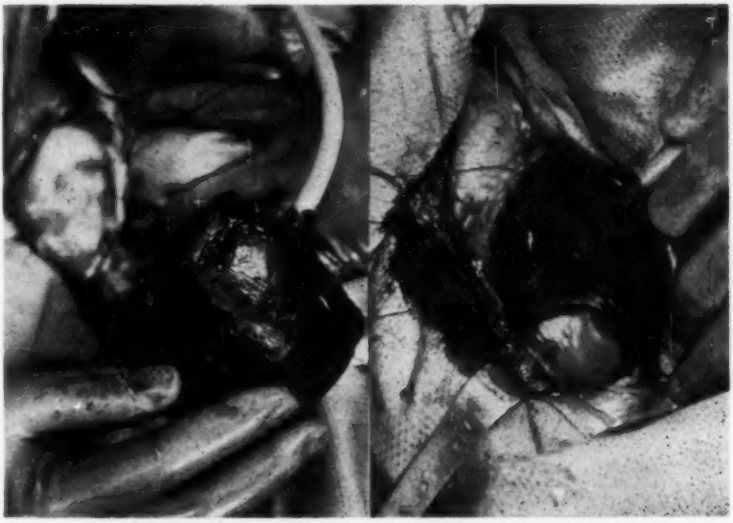

FIGURE 2A FIGURE 2B

FIGURE 2A: Rubber cuff ready to be applied around heart. The inflatable compartment is connected to the tube through which the air can be rhythmically introduced. FIGURE 2B: Rubber cuff applied around the heart with the inflatable compartment overlying the left ventricle.

is inflated by means of a double-action air pump controlled by a cam having a predetermined contour so that the pressure fluctuation of the flexible bag is divided into (a) one-third pressure stroke and (b) two-thirds suction stroke per revolution. This corresponds to the one-third systolic contraction and the two-thirds diastolic relaxation of the normal heart cycle. An average rate of 80 beats per minute was found to be optimal.

Procedure

These experimental studies were made on 21 mongrel dogs. The procedures carried out in each of these dogs were the same and can be summarized as follows: an intravenous cannulation was made to which 500 ml. of normal saline was connected and used later for addition of drugs. The dog was anesthetized using thiopentol sodium (Sodium Pentothal), oxygen and endotracheal tubing. Respiration was maintained by intermittent positive pressure, and electrocardiographic leads were then connected. The dog was placed on the right side and the left thoracic cavity was entered through the fifth intercostal space. The femoral and pulmonary arteries were catheterized with polyvinyl tubing and linked to P-23-d- Statham gauges. Pressures were monitored on a four channel Grass polygraph recorder. The lung was retracted laterally and the pericardial sac was opened and holding sutures were applied to the edges of the pericardium. The heart was delivered (Fig. 2) outside the pericardial sac and the bag applied. Cardiac asystole was produced with an electrical shock, using 75 volts A.C. The air then was introduced into the bag through the tube. The air pressure was adjusted and maintained when a maximum systemic pressure was reached. The pericarcardium was approximated and the sutures were loosely tied around the bag to help maintain it in position. Five minutes before the end of the experiment 4 ml. of Levophed in 500 ml. of normal saline was connected to the intravenous cannula and introduced slowly. The bag was removed and the heart defibrillated using 140 volts A.C. After the heart had been started, a period of at least 15 minutes was allowed to elapse, during which time the heart could be observed before the chest was closed. In our experience after ten minutes of efficient contraction the heart was not likely to stop again.

Result

Twenty-one dogs were used for these studies (See Table 1). The duration of cardiac compression ranged between 20 and 120 minutes. Nineteen dogs survived the procedure, one dying of anesthesia and the other of

TABLE 2—SYSTEMIC AND PULMONIC ARTERIAL PRESSURES MAINTAINED IN 21 DOGS OVER PERIODS UP TO TWO HOURS

	Duration in Min.	Systemic Pres. mm.Hg		Pulmonary Pres. mm.Hg		Postoperative Status
		SD	Mean	SD	Mean	
Maximum	120	100/60	75	40/23	35	19 Alive and well
Minimum	20	50/25	30	25/12	15	2 Dead of anesthesia
Average	47.6	73/40	50	30/18	22	

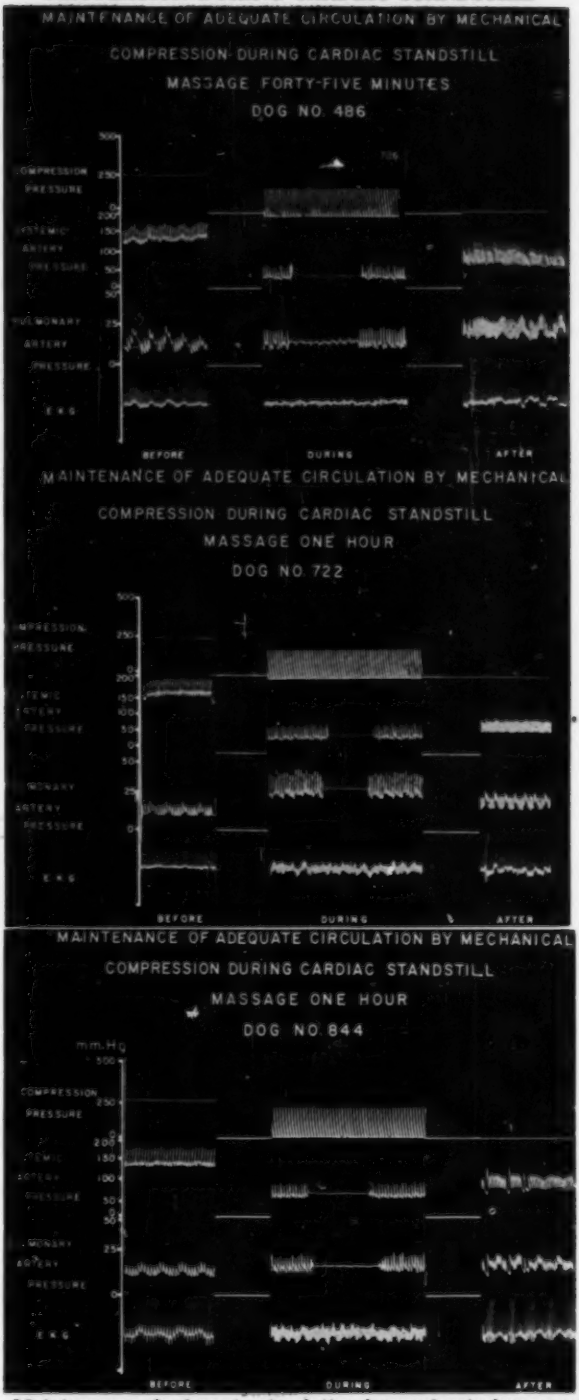

FIGURE 3: Maintenance of adequate circulation by mechanical compression during cardiac standstill for periods of (A, upper) 45 minutes; note systemic pressure of 80/40 with a mean of 50 mm.Hg. (B, center) 60 minutes; note systemic pressure of 70/35 with a mean of 50 mm.Hg. (C, lower) 60 minutes; note systemic pressure of 90/50 with a mean of 65 mm.Hg.

drug over dosage. Of the 19 surviving dogs, 14 were alive and well up to two weeks postoperatively and were sacrificed for pathologic studies. None of these revealed any sign of cerebral, pulmonary or cardiac disturbances. The five remaining dogs died between the second and tenth postoperative day from infection of the chest wall, pleura and pericardium, as a result of contamination at the time of surgery.

The following observations (See Table 2) were obtained during cardiac massage on the experimental animals: systemic pressures ranged from 55-100/30-60 with a mean of 30-75 mm. Hg. The pulmonary artery pressures were 25-40/12-3 with a mean of 15-35 mm. Hg. The air pressure necessary for this purpose ranged between 100-300 mm. Hg. Electrocardiographic tracings made before and after massage showed a return of normal rhythmical beats with little or no change in pattern.

Pathologic studies of lung tissue obtained before, immediately after and two weeks postoperatively showed essentially normal parenchyma except for an occasional minimal inflammatory reaction.

Discussion

In the interpretation of the systemic pressures obtained with mechanical compression of the heart, the mean arterial pressures were of most significance. As shown in Table 1, some dogs showed a high systemic pressure while others showed low pressures. Dogs that showed a comparatively low mean systemic and pulmonary pressure did equally well after surgery, these hypotensive pressures did not appear to influence the outcome of surgery since blood volume was maintained at a normal level. The use of hypotensive medication in major surgical procedures agrees favorably with these findings.

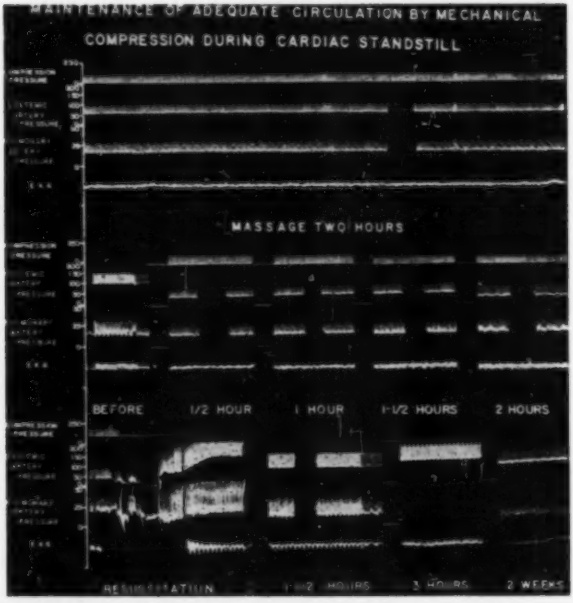

FIGURE 4: Maintenance of adequate circulation by mechanical compression during cardiac standstill for two hours. Note systemic pressure of 90/50 with a mean of 65 mm.Hg. Period of resuscitation followed promptly by normal rhythm and pressures, one and one-half hours, three hours, and two weeks postoperatively.

It was of interest to note that in some dogs adequate circulation could be maintained with comparatively low systemic pressures if concomitant low pulmonary artery pressures were obtained.

In the early experiments the average duration of mechanical compression was between 20 and 30 minutes. However, because of the satisfactory results obtained, the duration of massage was progressively increased to 120 minutes. Figure 3 illustrates the satisfactory systemic and pulmonary artery pressures at different durations ranging from 45 to 60 minutes.

Technically it was observed that when the bag fit the heart rather snugly the air pressure needed to produce a satisfactory systemic pressure was comparatively low. An example is illustrated in Fig. 4, where the air pressure of 100 mm. Hg produced a systemic pressure of 90/50 with a mean of 65, a pulmonary artery pressure of 45/15 with a mean of 20. In this experiment the mechanical compression of the heart was maintained for two hours at the end of which time the myocardium appeared healthy and was easily restored to a normal rhythm.

Clinical Application

In view of these experimental results, it is our opinion that this device would be helpful in the management of clinical cases of cardiac arrest. For practical purposes, once cardiac arrest is established, the chest is entered and the heart is massaged manually. If cardiac action begins promptly, there is no indication for any additional interference. However, in conditions where massage has to be carried out for longer periods, the apparatus could be applied and massage could be maintained more efficiently by mechanical means.

In addition, it is possible that efficient mechanical cardiac massage may be helpful in cases other than cardiac arrest. For example, in surgical procedures for correction of congenital anomalies, conduction defects or acquired valvular disease, mechanical cardiac massage may be valuable in the restoration of normal cardiac rhythm. This technique might be substituted for manual cardiac massage which at times subjects the myocardium to trauma and imposes fatigue on the operator.

SUMMARY

A method has been devised by which adequate systemic circulation could be maintained by mechanical cardiac compression for as long as 120 minutes. For this purpose a compressible rubber cuff, the mechano-cardio pulsator, was designed. This consisted of an inflatable compartment making possible selective pressure over the left ventricle and indirectly much lower pressure over the right ventricle, thus obtaining a satisfactory high peripheral systemic and a low pulmonic pressure. Long periods of massage were maintained without ill effect to the cerebral, coronary or pulmonary circulations. The myocardium could easily be restored to a normal rhythm at the end of the procedure. The possible clinical application of this method is discussed.

RESUMEN

Se ha ideado un metodo por el cual se puede mantener una adecuada circulación general mediante la compresión cardiaca mecánica por tan largo tiempo como 120 minutos. Para esto un manguito compresible de goma con un pulsador mecánico se ha construido.

Este consiste en un departamento inflable que hace posible la presión selectiva sobre el ventrículo izquierdo e indirectamente hacer mucho mas baja la presión sobre el ventrículo derecho obteniéndose así una satisfactoria elevada presión general periférica y una baja presión pulmonar. Se mantuvieron largos periodos de masaje sin malos efectors sobre las circulaciones pulmonar, cerebral o coronaria. El miocardio puede facilmente ser vuelto al ritmo normal al final del procedimiento.

Las aplicaciones clínicas posible son objeto de disertación.

RESUMÉ

Une méthode originale permet de maintenir pendant une période allant jusqu'à 120 minutes une circulation générale adéquate grâce à une compression cardiaque méchanique. Dans ce but, une manchette compressive en caoutchouc, le "mechano-cardio pulsator" a été réalisée. Elle consiste en un compartiment gonflable permettant une pression sélective sur le ventricule gauche, et indirectement une pression bien inférieure sur le ventricule droit; ceci permet d'obtenir de façon satisfaisante une forte pression dans la grande circulation, et une pression pulmonaire basse. De longues périodes de massage ont été maintenues sans effets nocifs sur la circulation cérébrale,

coronaire ou pulmonaire. A la fin de l'expérience l'état du myocarde permettait facilement de ramener un rythme normal. L'application clinique possible de cette méthode est envisagée.

ZUSAMMENFASSUNG

Es ist eine Methode entwickelt worden, mit deren Hilfe enie adëquate Zirkulation im großen Kreislauf für einen Zeitraum von nicht weniger als 120 Minuten durch eine mechanische Herzkompression aufrecht-erhalten werden konnte. Zu diesem Zweck wurde eine komprimierbare Gummimanschette entworfen, die als mechanischer Herzpulsator bezeichnet wird. Diese Manschette besteht aus einem aufblasbaren Teilstück, und dieses ermöglicht einen selektiven Druck über dem linke nVentrikel und auf indirektem Wege einen wesentlich geringeren Druck über dem rechten Ventrikel; auf diese Weise läßt sich ein befriedigender peripherer Druck im großen und ein niedriger Druck im kleinen Kreislauf erlangen. Es konnten lange Zeitspannen der Massage durchgeführt werden, ohne unangenehme Nebenwirkungen auf den cerebralen, coronaren bzw. pulmonalen Kreilauf. Das Myocard konnte dann leicht wieder am Ende des Eingriffes zu einem normalen Rhythmus veranlaßt werden. Diskussion der möglich klinischen Anwendung dieses Verfahren.

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OXYGEN POISONING UNDER WATER

In man, the inhalation of 100 per cent oxygen at ground level leads to the slow appearance of respiratory symptoms resembling progressive coryza. In skin diving during the breathing of oxygen, neurologic effects predominate and the reaction is accelerated. A concept is presented to implicate hyperventilation in "oxygen poisoning," with resultant symptoms of cerebral hypoxia. So many variables are involved that it is futile to speak of safe depth-exposure time during the use of oxygen-rebreathing equipment.

Burke, D. T.: "On Oxygen Poisoning under Water," *Med. J. Australia*, 1:693, 1961.

The Effect of Urea and Invert Sugar (Urevert) on Cerebral Damage Occurring After Cardiac Arrest*,**

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The human brain usually suffers irreversible damage if it endures anoxia for a period in excess of five minutes under normothermic conditions. Cardiac resuscitation techniques, properly applied according to present concepts, make it possible to restore the heart beat after long periods of anoxia, but the patient often dies or remains decerebrate as a result of the pathologic changes in the brain. Any method that will reduce the cerebral edema which follows cerebral anoxia will either prevent neurologic injury or decrease its severity. Hypothermia is beneficial in this respect, as shown by reports published by Williams and Spencer[1] in 1959, Zimmerman and Spencer[2] in 1959, Rosomoff *et al.*[3] in 1960, and Wolfe[4] in 1960. Urea has been shown to be an effective agent for reducing intracranial pressure and should be applicable to this syndrome. Fremont-Smith and Forbes,[5] in 1927, on the basis of experiments in which they injected 50 per cent urea intraperitoneally in three cats, suggested that urea might prove useful clinically. However, no clinical tests were reported prior to the study by Javid and Settlage[6] in 1956. Several experimental studies in dogs and rabbits indicated that urea is toxic when injected intravenously. Extensive clinical experience[7,8,11] along with experimental work on monkeys[9,10] resulted in the establishment of a technique for administering urea in combination with 10 per cent invert sugar.† This seems to be the treatment of choice in reducing intracranial tension in man. This appears to be the only combination that consistently does not produce hemoglobinuria. It consists of 70 ml. of 10 per cent invert sugar in water for each 30 grams of lyophilized urea. The usual dosage is 1 gram of urea per kilogram of body weight, but 1.5 gram per kilogram of body weight can be given safely. It was first believed that the diuretic effect of urea was the important factor in the reduction of cerebrospinal fluid pressure. However, Javid[11] observed that diuresis was not essential, especially in the early phase of cerebrospinal fluid pressure reduction, because there was a reduction in brain volume after intravenous injection of this urea solution at the time of operation, before there was any urinary output; also, there was a drop in cerebrospinal fluid pressure after administration of urea by gastric tube, before there was any diuresis. It appears that urea acts primarily on the basis of osmotic pressure differential between blood and cerebrospinal fluid, although the exact mechanism seems more complicated and requires further study. The two factors which limit the maintenance of cerebrospinal fluid pressure reduction are: (1) the rate at which the urea diffuses from the blood stream, and (2) the rate at which urea is ex-

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†The trade mark for this product is Urevert, manufactured by Travenol Laboratories, Inc., Morton Grove, Illinois.

creted. If the rate of elimination of urea can be decreased, the effect of a reduction in cerebrospinal fluid pressure is prolonged.

Only freshly prepared solutions should be used to avoid decomposition of urea when in solution due to aging. The recommended rate of intravenous administration is 60 drops per minute. Maximal effect occurs within one hour after administration. Reduction of intracranial pressure persists for periods of three to ten hours. Because of the marked diuresis, an indwelling catheter is placed before the urea is given and urinary output is measured.

On the basis of Javid's clinical and experimental evidence, we decided to test the effect of this solution on cerebral damage resulting from cardiac arrest (ventricular fibrillation) of five minutes' duration.

Experimental Method

Fifteen mongrel dogs, weighing 25 to 35 pounds, were used. Following a preoperative hypodermic injection of 0.8 mg. atropine, the dog was anesthetized with open ether technique, intubated with an intratracheal catheter and maintained during the operation on ether-oxygen anesthesia with the Rand-Wolfe Respirator. The left chest was shaved. A leg vein was cannulated and connected to a 500 ml. bottle of 5 per cent dextrose and water. The solution of urea, invert sugar and water was prepared. An incision was made through the fifth intercostal space. The heart was exposed and the pericardium was opened. Ventricular fibrillation was induced by shocking the heart with a small current from the electrodes of the Rand defibrillator. The corneal reflex disappeared within a few seconds, indicating that cerebral anoxia had developed. After exactly five minutes from the onset of fibrillation, the heart was pumped rhythmically by hand and the lungs were inflated with 100 per cent oxygen provided by the respirator. Hand pumping produced an effective circulation with a systolic pressure of 60 to 80 mm. Hg. When the muscle tone improved and the cyanosis in the heart disappeared, the heart was defibrillated by shocking it with 110 volts alternating current and 1.5-3.0 amperes. Defibrillation was usually difficult and required several shocks. During this period the heart was pumped by hand. As soon as a coordinated beat and a satisfactory blood pressure were obtained, the solution of urea, invert sugar and water was administered intravenously. The dosage used was 1.5 grams of urea per kg. of body weight, or 50 ml. of solution for a dog weighing 18 kg. This was given over a period of 90 to 120 minutes. It was repeated four times at three hour intervals. As soon as the chest was closed the intratracheal tube was disconnected from the respirator. The tube was left in place to provide an open airway. Morphine sulphate in one-half grain doses was given intramuscularly as needed to keep the dog quiet. After the fourth administration of urea and invert sugar in water was completed, the intratracheal tube was removed and the dog was returned to his cage.

A control group of 15 dogs was used. The anesthesia, the period of fibrillation and defibrillation were the same as in the other group. Urea invert sugar in water was not given. Morphine was given as in the other group.

Results

In the group of 15 dogs treated with urea, invert sugar and water the mortality was 11 (73 per cent); recovery without neurologic deficit occurred in four. Death occurred in the interval of 7½ and 40 hours with an average of 23 hours. These dogs were comatose during this period.

In the control series of 15 dogs, the mortality was 8 (53 per cent), recovery without neurologic deficit occurred in seven. Death occurred in the interval of one to 77 hours with an average of 32 hours. These dogs were comatose during this period.

SUMMARY AND CONCLUSIONS

Two groups of 15 dogs each were subjected to five minutes of ventricular fibrillation. Ventricular fibrillation stops all circulation. The brain was, therefore, subjected to a measured period of complete anoxia. The circulation was restored on the second after five minutes. This was done by hand pumping of the heart and by mechanical insufflation of the lungs with oxygen. The coordinated heart beat was restored. One test-group of dogs was given a solution of urea and invert sugar in water intravenously as soon as the period of anoxia was terminated. Otherwise the management of each group of dogs was the same. The conclusion is that intravenous administration of urea, invert sugar and water did not protect the dog after measured periods of cerebral anoxia. The mortality in the treated group was higher than in the untreated group. According to these experiments urea does not have the same beneficial effect as does hypothermia and it is not a replacement for hypothermia after resuscitation of the heart.

The effect of hypothermia was published. It was determined in two groups of ten dogs each. The dogs in each series were given either promethazine or chlorpromazine in addition to morphine or meperidine to prevent shivering. There were no recovery dogs in the control group. There were three recoveries in the group under hypothermia and the survival period before death was longer in this group. The results in these two series of dogs, cooled and not cooled, are not the same as in the control series reported in this paper. The conclusion is that promethazine and chlorpromazine contributed to death in each series of dogs. The increased death rate seems to be significantly greater when these drugs were used.

RESUMEN

Se sujetaron a cinco minutos de fibrilación ventricular dos grupos de 15 perros cada uno. La fibrilación ventricular detiene toda la circulación. Por tanto el cerebro sufrió un periodo medido de completa anoxia. La circulación se restableció en el primer segundo despues de cinco minutos. Esto se obtuvo por el bombea a mano del corazón y por la insuflación mecánica de los pulmones, con oxígeno. Los latidos coordinados del corazón se recuperaron. Un grupo de la prueba recibió una solución de urea y azucar invertida en agua por via intravenosa tan pronto como el periodo de anoxia terminó. Fuera de esto el manejo de los dos grupos fué el mismo.

La conclusión fué que la administración intravenosa de urea, azucar invertida y agua, no protegió al perro después de periodos medidos de anoxia cerebral. La mortalidad en el grupo tratado fué mayor que en el no tratado. De acuerdo con estos experimentos la urea no tiene los mismos efectos benéficos que tiene la hipertermia y no es un substituto de la hipotermia para la resucitación del corazón.

El efecto de la hipotermia fué publicado. Se determinó en dos grupos de 10 perros cada uno. Los perros de ambas series recibieron ya sea prometazina o cloropromazina además de morfina o meperidina para evitar el temblor. No se recuperó ninguno de los perros del grupo de control. Hubo tres recuperaciones en el grupo bajo hipotermia y el periodo de sobrevida antes de la muerte fue mayor en este grupo. Los resultados de estos dos grupos de perros, enfriados y no enfriados, no son los mismos como en las series de contro lrelatados en este trabajo. La conclusión es que la prometazina y la cloropromazina contribuyeron a la muerte de ambas series de perros.

El aumento en la proporción de las muertes parece significadamente mayor cuando estas drogas se usaron.

ZUSAMMENFASSUNG

Je 2 Gruppen von 15 Hunden wurden bis zu einem 5 Minuten dauerndem Kammerflimmern unterzogen. Kammerflimmern bringt den ganzen Kreislauf zum Stehen. Das Gehirn war daher einer beschränkten Zeitspanne einer kompletten Anoxie unterworfen. Nach 5 Minuten wurde der Kreislauf wieder in Gang gebracht. Dies gaschah durch Herzmassage von Hand und durch mechanische Zufuhr von Sauerstoff in die Lungen. Der koordinierte Herzschlag wurde wiederhergestellt. Eine Testgruppe von Hunden erhielt intravenös eine wässrige Lösung von Harnstoff und Invert-Zucker,

sobald die Periode der Anoxie beendet war. Sonst war die Behandlung einer jeden Gruppe von Hunden die gleiche. Es läßt sich daraus der Schluß ziehen, dass intravenöse Zufuhr von Harnstoff, Invert-Zucker und Wasser den Hund nach bestimmten Perioden cerebraler Anoxie nicht schützte. Die Mortalität in der behandelten Gruppe lag höher als in der nicht behandelten Gruppe. Gemäß diesen Experimenten hat Hamstoff nicht den gleichen nützlichen Effekt wie die Hypothermie und stellt keinen Ersatz für die Hypothermie nach Wiederbelebung des Herzens dar.

Der Effekt der Hypothermie wurde veröffentlicht. Er wurde an 2 Gruppen von je 10 Hunden bestimmt. Die Hunde in jeder Gruppe erhielten entweder Promethazin oder Chlorpromazin zusätzlich zu Morphium oder Meperidin, zur Vermeidung von Schüttelfrösten. In der Kontrollgruppe erholte sich kein Tier. In der Gruppe unter Hypothermie erholten sich 3 Hunde, und die Überlebenszeit vor de mTod war in dieser Gruppe länger. Die Resultate bei diesen 2 Serien von Hunden, unterkühlt und nicht unterkühlt, sind nicht die gleichen wie in den Kontrollreihen, über die hier berichtet wird. Es läßt sich daraus schliessen, daß Promethazin und Chlorpromazin in jeder Versuchsreihe von Hunden zum Tod beitrugen. Die erhöhte Zahl von Todesfällen scheint signifikant größer, als wenn diese benutzt wurden.

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INFLUENCE OF TUBERCULOSTATIC DRUGS AND ADRENOCORTICAL HORMONES ON ALLERGIC REACTION OF SKIN AND BLOOD IN TUBERCULOUS PATIENTS

The investigations were carried out on 81 tuberculous patients and 55 healthy persons who served as controls. In all, 481 tuberculin reaction tests were performed; the average period of followup was ten months.

The findings showed that in tuberculosis of adults, in cases with an acute course, allergic response is in conformity with the general allergy of the body. In 82 per cent of the cases of exacerbation of chronic tuberculosis, unfavorable changes in skin allergy preceded by several months the clinical relapse. Routine chemotherapy does not have any determined and constant influence on the character of the tuberculin skin reactions. Adrenocortical hormones seem to influence allergic response: there appears a trend to shift the body responsiveness towards prevalence of immunity over hypersensitivity; this can be simultaneous with clinical improvement in two-thirds of the cases.

Results of skin tests did not show characteristic differences between healthy persons and tuberculous patients.

Rozewska, M.: "Influence of Tuberculostatic Drugs and Adrenocortical Hormones on the Allergic Reaction of the Skin and Blood in Tuberculous Patients," *Gruzlica*, 28:333, 1960.

SUMMARY OF CURRENT THERAPY

Cardiac Arrest: Modern Management

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Arrest of cardiac function by ventricular fibrillation or asystole causes a cessation of all circulation. Immediate and vigorous resuscitative measures must be instituted since irreversible brain damage from anoxia can occur within four minutes.[1] This catastrophe occurs in a wide variety of conditions. Consequently, it is important that everyone concerned be acquainted with known precipitating factors of cardiac arrest, as well as with current methods of prevention, diagnosis and treatment. Skillful use of the newer resuscitative techniques can prevent crippling brain damage and death.

A. ETIOLOGY

1. *Primary Heart Disease:*

Cardiac arrest is usually seen in patients with ischemic heart disease, but it may occur in its absence.[2,3] When due to ischemia, ventricular fibrillation and asystole occur with equal frequency.[4] Coronary arteriosclerosis can effect the atrioventricular node and cause intermittent complete heart block with periods of ventricular arrest and, uncommonly, fibrillation. These episodes, commonly referred to as Stokes-Adams attacks, are characterized by apnea, cyanosis and clonic twitching of the muscles of the face and limbs. Death occurs unless A-V conduction reappears or an ectopic focus in the ventricle takes over pacemaker function, or unless resuscitation measures are successful.

Sudden cardiac arrest may develop suddenly in other forms of heart disease such as aortic or pulmonary valvular stenosis, atrial or ventricular septal defects, severe mitral stenosis, paroxysmal atrial and ventricular tachycardia, cardiac tamponade, massive pulmonary embolism, dissecting aneurysm, pericarditis and myocarditis.[1-4,5]

2. *Neurogenic Reflex*

Cardiac arrest may be precipitated by excessive reflex vagal action. Although experimental evidence suggests this is seldom the cause of cardiac arrest in normal hearts, vagotonia appears to be a significant contributing factor when ischemic heart disease is present.[3] Accordingly, caution should be exercised in those clinical activities where increased vagotonia may occur, such as carotid sinus massage, ocular pressure from eye bandages following ophthalmologic surgery, endoscopic examinations such as sigmoidoscopy, bronchoscopy and gastroscopy and manipulation of nerves and viscera during cervical, thoracic and abdominal surgery. Cardiac arrest has even been known to result from such a trivial procedure as vena puncture. The precise cause for this

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exaggerated response to vagal stimulation in patients with heart disease is not altogether known.

3. *Anesthesia*

Certain anesthetic gases are known to predispose to the development of ventricular fibrillation. This is particularly true when cyclopropane is used with epinephrine. However, other anesthetic gases including ether, nitrous oxide and chloroform may lead to increased myocardial irritability during surgical procedures.[6] Hypotension and anoxia cause increased myocardial irritability and must be avoided, particularly in patients with ischemic heart disease or those operations where autonomic stimulation, catecholamine release or direct stimulation of the heart may be anticipated.

4. *Direct Stimulation*

Operative manipulation of the myocardium which may lead to ventricular fibrillation or cardiac asystole is unavoidable in many thoracic and cardiac operations. Hypothermia increases the risk of ventricular fibrillation. However, these risks have been reduced to a minimum by new heat-exchange techniques and treatment of electrolyte disturbances associated with hypothermia and extracorporeal circulation. Direct stimulation of the heart during cardiac catheterization also carries a definite risk of inducing fatal ectopic arrhythmias or heart block.

5. *Anaphylaxis*

Anaphylactic reactions lead to cardiac arrest and, therefore, precautions must be taken to inquire and test for sensitivity before the administration of diagnostic contrast media during radiologic examinations, penicillin, mercurial drugs, aminophylline, and locally injected anesthetic drugs. Foreign protein biologicals such as anti-tetanus serum are well known for their allergenic properties and the occurrence of profound circulatory collapse or cardiac arrest.

6. *Electric Shock*

High voltage electric shock from accidental contact, electro-shock therapy or lightning discharge can cause cardiac arrest. Again, the presence of underlying heart disease or some other factor leading to increased myocardial irritability renders cardiac arrest more probable.

7. *Anti-arrhythmic Drugs*

Ventricular fibrillation may result from over-zealous treatment with all the so-called "anti-arrhythmic drugs" including quinidine, procaine amide, digitalis and prostigmine. Electrocardiographic signs of conduction delay or increased irritability of the myocardium due to the drug must be detected before each subsequent dose since these electrocardiographic signs precede the fatal event. During the transition from partial to complete heart block, the myocardium may be suppressed by these drugs so that asystole results.

8. *Electrolyte Disturbances*

Hyperkalemia probably is the important common denominator in the genesis of many types of cardiac arrest. It has been shown that potassium is a major excitant factor in the development and maintenance of ventricular fibrillation after experimental coronary occlusion.[7] Similarly, a recent clinical study demonstrated that potassium intoxication from the rapid infusion of large quantities of bank blood, together with the release of endogenous hepatic potassium due to hypoxemia, could cause cardiac arrest.[8] In this regard, it is interesting to note that both anoxia and hypercapnia are powerful stimulants to the reflex release of cellular potassium, particularly from the liver. Cardiac arrest due to hyperkalemia may occur because of release of intracellular potassium during breakdown of red cells in sickle cell anemia and during the administration of potassium in electrolyte replacement therapy. Conversely, hypokalemia from prolonged vomiting, diarrhea, gastric suction, primary aldosteronism, chronic potassium losing nephritis, glucose and insulin therapy for diabetic ketosis, during sodium cycle cation exchange resin therapy or the prolonged use of a diuretic without potassium supplementation, may also cause increased cardiac irritability, particularly during digitalis therapy.[9]

9. *Hypoxemia*

Hypoxemia may result from central depression of the respiratory centers in the medulla, interference with the oxygen carrying capacity of the blood or from mechanical obstruction of the airway due to aspirated vomitus, drowning, foreign bodies or inspissated bronchial secretions. Severe and prolonged hypoxia frequently causes gradual lengthening of the A-V and intraventricular conduction, leading to complete heart block and asystole. Ventricular fibrillation may supervene terminally or develop suddenly during the hypoxia. When sudden rebreathing abruptly lowers the blood carbon dioxide tension, ventricular fibrillation may develop.[5] There is experimental evidence to indicate that changes of the arterial pH, rather than carbon dioxide tension, are a more important cause of cardiac arrest in the hypercapneic states. The production of electrical instability of the heart because of local oxygen gradients within the myocardium has been considered to be a cause of sudden ventricular fibrillation. It is almost impossible to resuscitate a patient with cardiac arrest unless oxygenation is assured by effecting an adequate airway.[4]

B. DIAGNOSTIC CONSIDERATIONS

Cardiac arrest may appear with few, if any, premonitory signs or symptoms. Initially, it may resemble a vaso-vagal syncope. However, unlike a simple "faint," cardiac arrest is associated with absent or gasping respirations, deep cyanosis, dilatation of the pupils and clonic twitching of the muscles of the face and limbs. Confirmation of the diagnosis is made by the absence of heart sounds, precordial pulsations, radial pulse, and later, apnea. Electrocardiograms are rarely made as part of the initial diagnostic procedure since time does not permit delay. It is important, however, to obtain an electrocardiogram at the earliest possible moment for purposes of determining if cardiac arrest is due to

asystole or ventricular fibrillation and for continuous monitoring during the resuscitative procedure.

In those situations where cardiac arrest appears to be impending or risk of its appearance is great, electrocardiographic monitoring is also essential. A few clinical observations can be regarded as signs of impending disaster. These signs include increasing respiratory embarrassment, increased frequency of ectopic ventricular premature contractions, bradycardia and paroxysmal atrial or ventricular arrhythmias.

The differential diagnosis of cardiac arrest is essentially that of sudden loss of consciousness such as vaso-vagal syncope, epileptic seizures, trauma, or intra-cranial bleeding. It is important that the differential diagnosis should be made as quickly as possible so that resuscitative measures for cardiac arrest may be instituted before the four minute time elapses. On the other hand, while speed is essential, judgement is all important. In one instance, a physician suffered a syncopal episode while watching an operation. The surgical staff immediately opened the chest to attempt resuscitative measures and, to their consternation, found the heart was beating normally. A moment of careful examination would have avoided the unnecessary risk of thoracotomy and a painful, prolonged convalescence.

C. MANAGEMENT

Thoracotomy with cardiac massage has been used for some time in the management of sudden cardiac arrest.[8] While this procedure is entirely practical within the operating room, it presents formidable problems in many other locations. It is probable that the anticipation of vigorous bleeding and a struggling patient upon return of consciousness may deter some practitioners from using this technique in public places. These drawbacks have been solved largely by the introduction of closed-chest massage and mouth-to-mouth respiration. The details of this ingenious technique are described elsewhere.[9] When properly applied, the otherwise brief four minute interval between the time of cardiac arrest and irreversible brain damage has been prolonged considerably. This technique maintains a circulation and thus makes available time for a more accurate total assessment and transportation of the patient to hospital where definitive measures may be taken to restore normal cardiac action. The simplicity of closed-chest cardiac massage has led to its wide-spread acceptance. It should also be appreciated that overzealous compression of the thorax and heart during this technique may result in multiple rib fractures, hemopericardium, hemothorax, cardiac rupture, hematoma of the liver and bone marrow emboli to the pulmonary arteries.[10,11] These adverse sequelae, however, should not discourage attempts at cardiac resuscitation where it is indicated, but they do serve to emphasize the need for reasonable care. External cardiac massage can be administered effectively by a lone operator, alternating a few breaths of mouth-to-mouth respiration with rhythmic chest compression. It is evident that assistance is to be preferred, so that one operator maintains respiration while the other applies external cardiac massage. Positioning the patient in a slight (5° to 10°) Trendelenburg position will help promote cerebral circulation. Every effort should be made to remove the patient to a hospital at the earliest possible moment where

resuscitative equipment and the skilled assistance of a surgeon, anesthetist and cardiologist can be utilized fully.

Electrocardiographic monitoring is desirable during the resuscitation procedure. It should be emphasized that ventricular fibrillation requires electrical defibrillation and that good myocardial oxygenation is necessary for the electric shock to be effective. Resuscitative measures are ineffective unless the airway is clear for adequate oxygenation.[4] Spontaneous reversion of ventricular fibrillation to normal sinus rhythm has been known to occur without electrical defibrillation,[2] but this remote possibility should not delay attempts at defibrillation. If defibrillation with external electrodes is not effective, thoracotomy and direct placement of the electrodes on the heart will be necessary. Should repeated shocks fail to stop the fibrillation, 5 to 10 cc. of 1 per cent procaine hydrochloride may be injected into the ventricular cavity. Manual compression of the heart should be employed after the injection to continue circulation and deliver the drug to the myocardium. Repeat shocks may be attempted after the procaine injection. Should ventricular asystole occur after electrical defibrillation or procaine injection and manual compression does not initiate a spontaneous rhythm, 2 cc. of 1:10,000 solution of epinephrine or 1 cc. of 1:500 solution of isoproterenol (Isuprel) should be injected into the left ventricular cavity. Caution is required with epinephrine solution since this may contribute to the development of ventricular fibrillation.

Where cardiac arrest is due to ventricular asystole or standstill, a single vigorous blow to the anterior chest may reinitiate a rhythm. If this fails, external cardiac massage should be continued while additional attempts to restore activity of the heart are carried out. Epinephrine or Isuprel solution in the same concentrations previously described may be injected into the left atrium or left ventricular cavity. A heart that continues in standstill, despite epinephrine or Isuprel therapy, may respond to 4 cc. of 10 per cent calcium chloride solution injected into the left atrium or ventricular cavity. Intravenous sodium, molar lactate or 0.5 per cent atropine solution may be of benefit particularly when vagotonia is present. If spontaneous rhythm has not been obtained from these measures, an external or internal electrode cardiac pacemaker is required if life is to be saved.

D. PROGNOSIS

The probability of survival after cardiac arrest depends largely on the cause of the arrest, the underlying disease, the patient's age, and the rapidity with which resuscitative measures are instituted. It is evident that in some patients when heart action ceases, judicious inactivity on the part of the attending medical staff is warranted. These include many chronic or irretrievable clinical situations where death comes not as an enemy but as a friend, and others where the interval from arrest to initial resuscitative effort is not compatible with life.

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DILATATION OF ASCENDING AORTA AND AORTIC SINUS

The angiocardiographic study a year after resection of a coarctation and end-to-end anastomosis of the aorta in a 14-year-old schoolgirl revealed subsidence of the dilatation of the aortic sinus and ascending aorta. These data suggest that such changes may be due to hypertension, the correction of which permits the structures to return to normal. Thus, operation early in life and before too prolonged aortic stretching has occurred is desirable.

Leider, H. J., and Steinberg, I.: "Subsidence of Dilatation of Ascending Aorta and Aortic Sinus after Resection of Coarctation," *J. Thor. and Cardiov. Surg.*, 41:670, 1961.

PULMONARY ARTERIAL PRESSURE IN MITRAL STENOSIS

By means of chest roentgenograms and pulmonary artery catheterization, correlations were obtained between 51 measurements of mean resting pulmonary arterial pressure and certain quantitative roentgenologic variables in 48 patients. With the use of statistical methods, several objective roentgenologic parameters for the determination of pulmonary arterial pressure were investigated. Regression equations were divided which gave a strong correlation ($r = +0.87$) between mean resting pulmonary arterial pressure and four roentgen parameters: the presence or absence of Kerley's B-lines, the high in millimeters of the pulmonary artery segment, the width in millimeters of the right descending pulmonary artery branch, and the "pulmonary arterial size" in centimeters. Methods described by others for quantitation of pulmonary arterial pressure by roentgenologic measurements were found to have lower degrees of correlation when applied to the group of patients examined.

Johnson, P. M., Wood, E. H., Pasternack, B. S., and Jones, M. A.: "Roentgen Evaluation of Pulmonary Arterial Pressure in Mitral Stenosis," *Radiol.*, 76:541, 1961.

ELECTROCARDIOGRAM OF THE MONTH

Edited by Stephen R. Elek, M.D.

Fluctuating Nodal Rhythm

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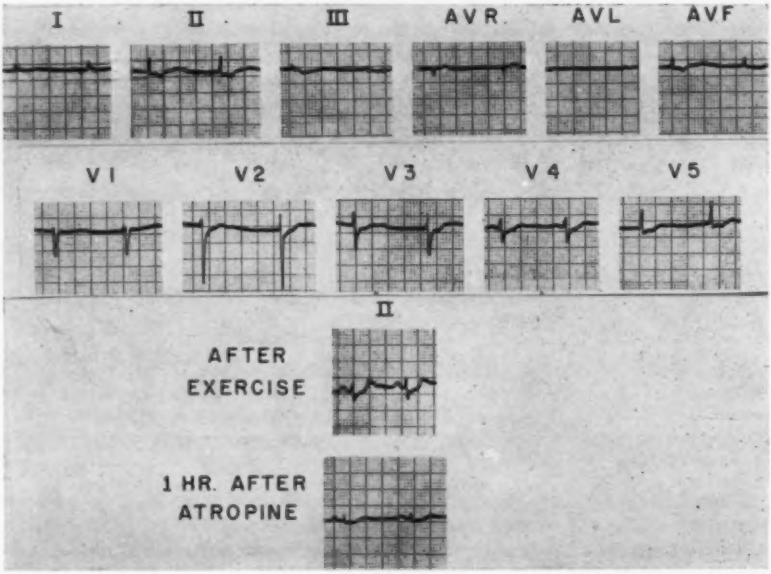
A 44 year-old accountant was admitted to the Gülhane Military Medical Academy complaining of symptoms which proved to be diabetes mellitus. He had no cardiac symptoms and no impairment of cardiovascular reserve. His blood pressure was 140/80 mm. Hg. He was obese. His fasting blood sugar was 345 mg. per cent and his blood cholesterol was 200 mg. per cent. Systemic and cardiac physical examination was normal. X-ray film of the heart and lungs was normal. There was no evidence of anemia. His family history was negative for cardiovascular disease.

The control electrocardiogram shows a heart rate of 68 beats per minute with P waves notching the ST segment. These retrograde P waves also account in part for the appearance of ST segment depression best seen in Leads V_2 - V_5. In Lead V_4 the rhythm becomes normal sinus with a heart rate of 75 beats per minute. This often indicates that the tone of the vagal innervation of the atria fluctuates. This idea can be tested by maneuvers which alter the vagal tone, such as exercise and the



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intravenous administration of 1 mg. of atropine. Both of these procedures (see illustration) result in normal sinus rhythm, that is, abolition of the nodal rhythm. After exercise (double Master's test), the morphology of the ST segment is of the "ischemic" type suggesting that the electrocardiogram may not be normal. The latter abnormality, on the other hand, may be due to the uncontrolled diabetes and may disappear when this disease is treated.

This electrocardiogram illustrates that the vagal influence upon the atrial rhythm may fluctuate more than normal, but this by itself is not abnormal when the presence of varying vagal tone is confirmed by exercise and intravenous atropine.

OBSERVATIONS ON CROSS REACTIONS OCCURRING BETWEEN TUBERCLE BACILLI AND BRUCELLAE

In trying to clear up the nature of cross reactions observed in agglutination tests between sera of patients with tuberculosis and brucellosis, the authors performed hemagglutination reactions (Middlebrook and Dubos) using polysaccharide antigen from *Brucella* and from tubercle bacilli on 45 sera from tuberculosis patients and 25 sera from patients with brucellosis.

Tuberculous sera gave positive reactions with polysaccharide antigen from *Brucella*; the opposite was also observed, i.e., sera from patients with brucellosis gave positive reactions with polysaccharide antigen from the tubercle bacillus. The number of these reactions and their intensity were low.

Serpa, C. E. V., and Fuks, M. A.: "Observations on Cross Reactions Occurring between Tubercle Bacilli and Bruceilae," *An. de Microbiologia*, 8:169, 1960.

EVALUATION OF CARDIOVASCULAR CONTRAST MEDIA

Viscosity, catheter flow rates and densitometry of the several radiopaque media commonly used for intrathoracic cardiovascular opacification procedures have been studied. Animal tolerance studies indicate that the diatrizoate compounds are less toxic than the lodopyracet (Diodrast 70 per cent) or acetrizoate (Uorokon 70 per cent) compounds.

The combination of relatively easy injectability, comparatively low toxicity, moderate radiodensity and a possible lower incidence and degree of undesirable reactions appears to favor those contrast media containing a moderate rather than a high concentration of diatrizoate compounds. This combination, particularly the lower toxicity, definitely favors these moderate-concentration diatrizoate solutions over the lower-viscosity but more toxic lodopyracet and acetrizoate media. Clinical experiences, espeically the incidence and extent of untoward reactions observed in intrathoracic cardiovascular opacification studies with sodium diatrizoate (Hypaque-M 75 per cent), sodium diprotrizoate 31.4 per cent (Diktriokon) and sodium diatrizoate, 35 per cent (Renovist) are tabulated. The authors are favorably impressed with the overall infrequency of undesirable reactions with these media.

Lehman, J. S., and Debbas, J. N.: "An Evaluation of Cardiovascular Contrast Media," *Radiol.*, 76:548, 1961.

Melioidosis*

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Melioidosis is an infectious disease caused by a glanders-like bacillus, *Malleomyces pseudomallei*. It usually produces an acute generalized septicemic clinical picture, with multiple miliary and diffuse abscesses and with early death. Rarely, a chronic course is seen with multiple sinuses of the soft tissue which is very similar to glanders. About 300 cases have been reported to date almost all of these were from Far Eastern countries. In acute forms, symptoms of the clinical picture may resemble different infectious diseases such as malaria, typhoid fever, cholera, glanders or bronchopneumonia.

The disease was first discovered and the organism identified in Rangoon (Burma) by Whitmore and Krishmahwami in 1912. It was seen among people who were using morphine by primitive and non-sterile methods of injection. The disease was initially diagnosed as glanders. Bacteriologic studies of sputum, abscess material, and blood revealed another organism, however, which was called a "glanders-like bacillus." In 1921, at the Conference on Tropical Disease (Batavia), this new organism was named *Bacillus Whitmore*, and the disease, melioidosis. In 1918, this organism was identified during bacteriologic studies of specimens taken from a cat. In 1925, Stanton and Fletcher isolated it from the liver and spleen of a dog which had died with jaundice, diarrhea and generalized suppurative lesions. They also found the micro-organism in the mucopurulent nasal secretion of a horse. In 1930, *Bacillus Whitmore* was isolated from a splenic abscess in a cow. Usually melioidosis is a primary disease of rodents, but it is often impossible to demonstrate it in rodents in the immediate area in which cases occur in human beings.

The first case from the western hemisphere was reported by McDowell and Varney in 1947 in the United States. This case presented with ulcers and sinuses of eight years' duration in the right buttock and thigh. The organism was recovered repeatedly from blood agar cultures of pus and tissue debris.

In 1952, another case was reported from Morocco. The patient was a cavalry officer who had served in Saigon prior to the appearance of his disease.

Our case was an individual from the southern part of Turkey who has never been out of this country. This is the first reported case of pulmonary melioidosis in western countries (Near East, Middle East, and Europe).

The mode of transmission has not been established, but great importance has been attributed to food and water contaminated with the excreta of infected rodents. Blanc and Baltazard have demonstrated experimentally that the disease can be transmitted by the *Aedes egypti* mosquito and the rat flea, *Xenopsylla cheopsis*. Human to human trans-

*Report of the first case of pulmonary melioidosis from the western countries.
**Professor of Medicine (Chest Diseases), Medical School, Ankara University, Turkey. Bacteriologic diagnosis was made by Dr. S. Payzin, Professor of Bacteriology; and Dr. K. Özsan, Assistant Professor of Bacteriology, Medical School, Ankara.

mission has not been reported. Others believe that contaminated water may be the vehicle of transmission through broken skin. In our case this was a probability.

The clinical course of melioidosis is much like glanders, but it is even more virulent, and lethal. Nearly all untreated cases have ended fatally.

Diagnosis: Early diagnosis of melioidosis is possible by bacteriologic and serologic methods, since Whitmore bacilli can be isolated from blood, sputum, exudate and urine. Straus' reaction can be used as a diagnostic procedure by intraperitoneal injection of infected material into male hamsters and guinea pigs. The agglutination and complement fixation tests become positive after two to four weeks.

The clinical picture of the disease is variable. Symptoms and signs may resemble several infectious conditions. Differential diagnosis can be accomplished only by bacteriologic methods.

Biopsy specimens reveal pathologic changes which are indistinguishable from those seen in glanders.

At necropsy, acute cases show generalized and disseminated miliary granulations with central necrosis. Subacute forms show diffuse multiple nodules, surrounded by a congested area, all over the body and viscera. Pulmonary localization is very similar to miliary tuberculosis. The spleen is enlarged, with septic infarctions. Suppurative lesions contain pus which is honey-like in color. Hepatic foci may imitate amebiasis. Suppurative lesions of the bones and muscles are not pathognomonic.

Prognosis: Melioidosis in its acute forms is usually fatal. Before antibiotics, the mortality rate of the disease was about 98-99 per cent. The longest follow-up recorded in the literature is eight years.

Our patient's survival period is over one year; he is still alive without any x-ray evidence of improvement.

Treatment: Good results have been reported with combined treatment using penicillin and sulfonamides. Sulfamerazine was given in doses of 2 gm. daily for a long period. Some strains of Whitmore bacilli were found to be resistant at therapeutic levels of streptomycin, penicillin, and sulfonamides *in vitro* tests. Oxytetracycline and chloramphenicol may be effective. *In vitro* sensitivity tests should be done before drug therapy, since susceptibility of the strains may vary considerably. Vaccines prepared with heat-destroyed bacteria were unsuccessful. Our patient was given chloramphenicol 1.5 gm. daily. His clinical signs improved and he gained weight; however, x-ray findings were unchanged. Since sensitivity tests with sputum showed some strains of bacteria sensitive to tetracycline, the patient was also given this drug for a period of time. He is still on these drugs alternately.

Case Report

N. Ö., a 52 year-old male grocer, entered the hospital on January 21, 1959. On admission, his chief complaints were cough, expectoration, and shortness of breath. One

TABLE 1—COMPLEMENT FIXATION TEST

Anti-malleus serum	1:2	1:4	1:8	1:16	1:32	Control
1:5	4	4	1	0	0	
1:10	4	3	1	0	0	
1:20	4	2	1	0	0	
1:40	4	2	1	0	0	

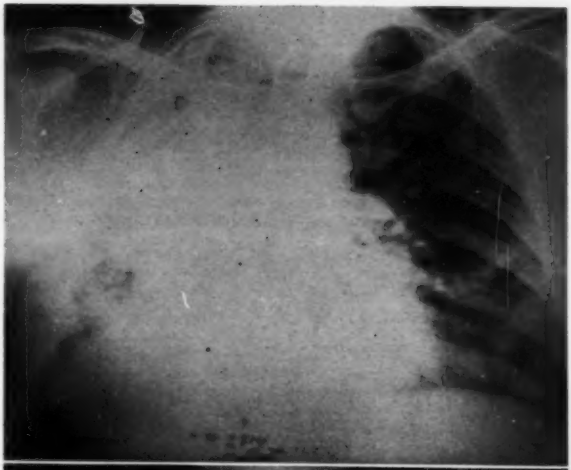

FIGURE 1

FIGURE 2

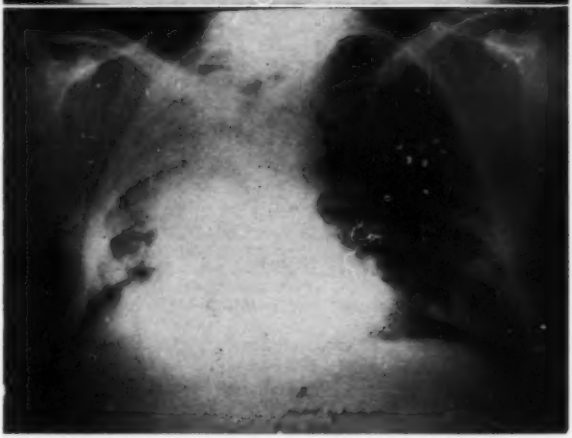

FIGURE 3

FIGURE 1 (upper): X-ray film of the chest on admission, September 28, 1958. FIGURE 2 (center): First control film, January 1, 1959. FIGURE 3 (lower): Second control film, February 3, 1959.

year before admission, his home in Adana, a town in southern Turkey, was flooded. He stayed in the water for many hours to save his family. Three months after the flood, he suddenly fell ill. He had chills, high fever, cough and shortness of breath. He was not acutely ill immediately, but his condition became quite serious. By the fourth week, diarrhea developed. He was diagnosed by his family doctor as having pneumonia. Then, since his condition did not improve, he was referred to his local hospital for admission. X-ray examination of the chest revealed some densities in the right lung. Sputum examination was negative for tubercle bacilli. After he failed to respond to treatment with antibiotics and because cancer of the lung was suspected, he was referred to our clinic. On admission to our clinic, he complained of easy fatigue, shortness of breath, sleeplessness, poor appetite, and cough. There had been no elevation of temperature.

Physical examination of the chest revealed percussion dullness in the right upper lung field. On auscultation, there were a few rales and bronchial breath sounds in this area. The other systems did not show any abnormality. The physical findings remained about the same throughout his hospital stay, but his general condition improved considerably and he gained weight.

A chest x-ray film taken on January 22, 1959, revealed asymmetry of the bony thorax. The intercostal spaces of the right hemithorax were narrower than the left. In the right lung there was a homogeneous shadow from the apex to base, and on the left side, some scattered densities were seen. X-ray films of the pelvis, extremities and the skull did not show any abnormality of skeletal structures. X-ray films of the chest taken every two weeks after his admission and while on antibiotic treatment, did show a slight radiologic improvement.

Bronchoscopy: Epiglottis, trachea and carina were found to be normal. The orifice of the main right bronchus was found to be hyperemic with purulent secretions. In the bronchial washings, neither atypical cells nor acid-fast bacilli were reported. The bacteriologic studies revealed an unusual bacterium and hemolytic streptococcus sensitive to the tetracycline hydrochloride.

Further bacteriologic studies summarized below confirmed Whitmore bacilli as etiologic agent of this clinical picture.

Growth Characteristics:

On nutrient agar: slightly viscid, yellow-brownish, both smooth and rough colonies (S and R forms) were grown.

In agar stab culture: aerobic, gray-yellowish, abundant growth was seen; it was extending slightly up the sides of the tube.

On blood agar plates: in rabbit—blood agar in 24 hours, in sheep—blood agar in 48 hours, hemolysis has been seen and greenish colonies were grown.

On Löffler's serum: confluent, butyrous growth, yellow in color, has been observed. It liquefied the media within two to four days.

In nutrient broth: growth in this medium was characteristic. The bacilli formed a thick butyrous surface pellicle, which tended to precipitate spontaneously and formed a deposit and this pellicle partly extended up the sides of the tube. There occurred a slight turbidity and the color of the medium turned yellow.

In peptone water: same as in nutrient broth.

In gelatin stab: liquefication was observed on the seventh days.

In milk: a soft clot was formed in eight days.

On potato: first a cream-colored, later a yellowish growth was seen.

Identification of the causative microorganism is corroborated by specifications given by those findings shown in Table 1 compared with the characteristics of *Pseudomonas pseudomallei* given by Bergey, Haudoroy,** and Topley and Wilson.†

Morphology and serology: Bacillus was Gram-negative, actively motile. The yellow pigment which was formed by this bacillus was not soluble in either chloroform nor in water (this differentiates it from *Pseudomonas aeruginosa*). With all these characteristics it seemed that it would probably be one of the members of *Pseudomonaceae*. Also, serological tests confirmed that the bacillus was *Malleomyces pseudomallei*. An agglutination test with anti-malleus diagnostic serum revealed a delayed positive reaction with the bacillus (1:160, ++ and 1:320, + in titer). Complement-fixation test with anti-malleus serum did show the results as in Table 1.

Animal experiment: A guinea pig was inoculated with 2 cc. of broth culture intraperitoneally; the animal died six days later. Necropsy findings were as follows: "Edema at the site of inoculation, enlargement of both inguinal lymph nodes, congestion of the visceral organs and secretion in serous cavities have been seen." Cultures and direct smears taken from different organs were found negative for the bacilli. The cause of death was toxemia."

Drug sensitivity: Bacillus was sensitive to chloramphenicol, the tetracycline group of antibiotics and erythromycin and resistant to penicillin and streptomycin.

The sputum of the same patient was negative for tubercle bacilli by culture and animal inoculations.

No abnormal findings have been seen in the other systems.

****Dictionaire Bacteriologique*, 1953.**

†*Principles of Bacteriology*, 1948.

SUMMARY

Melioidosis is an infectious disease caused by a glanders-like bacillus, *Malleomyces pseudomallei*. The organism usually produces an acute, generalized septicemic clinical picture with multiple miliary and diffuse abscesses with early death. Very seldom it causes chronic disease, with several sinuses in the soft tissues which are similar to the manifestations of glanders. About 300 cases have been reported to date. Almost all of them were from the Far East.

This paper reports the first case of pulmonary melioidosis in the Western hemisphere.

RESUMEN

La Melioidosis es una enfermedad infecciosa causada por el bacilo, semejante al del muermo, llamado malleomyces pseudomallei. Este gérmen produce generalmente una septicemia aguda con abscesos múltipes y miliares, y muerte temprana. Muy rara vez causa enfermedad crónica con varias fístulas en los tejidos blandos que son similares a los del muermo. Se han relatado alrededor de 300 casos hasta hoy. Casi todos han sido de Lejano Oriente. Este trabajo relata el primer caso de melioidosis pulmonar en el hemisferio occidental.

RESUMÉ

La mélioïdose est une maladie provoquée par un germe qui ressemble à celui de la morve, *malleomyces pseudomallei*. Cette bactérie cause généralement un tableau de septicémie aiguë généralisée, caractérisée par de multiples abcès miliares disséminés et une mort rapide. Très rarement, elle peut provoquer une maladie chronique avec multiples fistules des parties molles, semblables aux manifestations de la morve. Près de trois cents cas ont été rapportés jusqu'à présent. Presque tous provenaient de l'Extrême-Orient. L'auteur présente le premier cas de mélioïdose pulmonaire constaté en Occident.

ZUSAMMENFASSUNG

Die Melioidose ist eine Infektionskrankheit, die durch einen rotzähnlichen Bazillus hervorgerufen wird, *malleomyces pseudomallei*. Der Erreger bewirkt für gewöhnlich ein akutes generalisiertes septisches klinisches Krankheitsbild mit multiplen Milliaren und diffusen Abszessen und frühem tödlichen Ausgang. Sehr selten verursacht der Erreger ein chronisches Krankheitsbild mit verschiedenen Eiteransammlungen und Fistelbildung im Bindegewebe, die den Manifestationen der Rotzkrankheit ähnlich sind. Bisher liegen Berichte über etwa 300 Fälle vor. Die meisten von ihnen kamen aus dem fernen Osten. Die vorliegende Mitteilung berichtet über den ersten Fall einer pulmonalen Melioidose in der westlichen Hemisphäre.

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Abnormalities of the Pulmonary Artery Resembling Intrathoracic Neoplasms*

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The roentgen-ray finding of a mass in the chest presents a perplexing diagnostic problem. When this shadow has a smooth outer border and blends with the mediastinal structures, the differential diagnosis should include abnormality of the pulmonary artery. Angiocardiography is the quickest and the most accurate method of establishing or eliminating vascular abnormalities as the cause of such a shadow. Symptoms and physical signs may be absent or confusing. Fluoroscopy, laminography, bronchography, and bronchoscopy may fail to differentiate the vascular lesions. Under these circumstances, suspicion of the existence of a vascular lesion and the performance of angiocardiography can make an exploratory thoracotomy unnecessary.

Angiocardiography has been used to differentiate between aortic aneurysms,[1] pulmonary artery enlargements,[2] and malignant intrathoracic structures.[3] The increasing use of chest x-ray film survey programs and the ready availability of thoracotomy have increased the importance of accurate diagnosis. Angiocardiography is a procedure available to physicians and surgeons dealing with chest diseases. This paper presents a brief summary of our experiences in differentiations between intrathoracic neoplasms and abnormalities of the pulmonary artery. Routine x-ray films, angiocardiograms, and clinical histories illustrate the salient features.

Material and Methods

The angiocardiograms were performed using a serial film changer. The contrast medium (usually warm diatrizoate sodium [90 per cent Hypaque]) was injected either through a Robb-Steinberg cannula into an antecubital vein, or through a Lehman catheter inserted into the right heart. All of the patients presented radiologic findings of a hilar mass with or without signs, symptoms, fluoroscopic, and bronchoscopic findings which led initially to a primary diagnosis of intrathoracic neoplasms. (Table 1).

Results and Discussions

Angiocardiography played a vital role in the differential diagnosis of abnormal shadows in the lung. Robb and Steinberg[4] in their early communications on angiocardiography described the uses of this procedure in chest diseases. They presented one case of distorted pulmonary artery due to tuberculosis in the left upper lobe which resembles our fifth case. Since that time, angiocardiography has become more widely used in the diagnosis of cardiac disease, particularly congenital cardiac disease. The pulmonary disease applications of angiocardiography have not been

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FIGURE 1: The mass in the left hilar region was interpreted as a bronchogenic carcinoma with secondary atelectasis in the left mid-lung field. Injection of diatrizoate sodium (Hypaque) through a catheter revealed the mass to be pulmonary artery associated with fibrosis and bronchiectasis in adjacent lung.

widely appreciated. Angiocardiography has been used to predict the operability of neoplastic lesions,[5] and was found to be of some value in the differential diagnosis of pulmonary neoplasms.[6] Pulmonary angiocardiography and simultaneous bronchography has been used to recognize preoperatively areas of absent lung function.[7]

In our material, abnormalities of the pulmonary artery that can be confused with intrathoracic neoplasm have been of two types. In the first type, there is a mediastinal mass with normal lung fields (cases 7 to 11), and in the second type the mass is associated with abnormal peripheral lung fields. The latter has been more common, (cases 1 to 6), and the associated lung pathology appears to contribute significantly to the production of an abnormal pulmonary artery. Congestive heart failure was present in four of these cases and further dilatation of the pulmonary arteries secondary to the failure may have contributed to the production of the abnormal x-ray shadow. It was necessary to make multiple diagnoses in these cases, such as bronchiectasis, associated

FIGURE 2: This 83 year-old man was thought to have bronchogenic carcinoma in the right upper lobe with distal atelectasis until angiocardiography revealed the mass to be an elevated pulmonary artery due to upper lobe fibrosis.

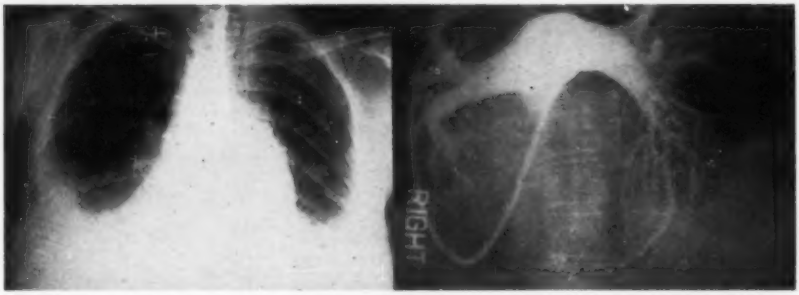

FIGURE 3: This 52 year-old woman was thought to have mediastinal neoplasm with pleural metastasis. The angiocradiogram proved the mediastinal masses to be pulmonary arteries and catheterization data established constrictive pericarditis as the cause of the pleural effusions.

dilatation of the pulmonary artery, and congestive heart failure. Of the remaining cases that were not in congestive heart failure at the time of the examination (cases 7 to 11), two had congenital intracardiac shunting, (cases 6 and 10), two idiopathic dilatation of the pulmonary artery, and one poststenotic pulmonic dilatation. In this second group, the abnormality was confined to the pulmonary artery and the lung fields were normal.

Greenberg[4] has defined idiopathic dilatation of the pulmonary artery as a simple dilatation of the pulmonary artery with the absence of shunting, no evidence of cardiac or pulmonary disease, and no intrinsic disease of the pulmonary artery. The recognition of this entity is usually not difficult and two of our cases actually were idiopathic dilatation of the pulmonary artery. We have encountered this entity on other occasions, but these cases were the only ones which were actually thought to have a neoplasm. Pulmonary artery aneurysm has been defined by Deterling[5] as the finding at necropsy of "a permanent more or less circumscribed dilatation of the pulmonary artery with some degeneration

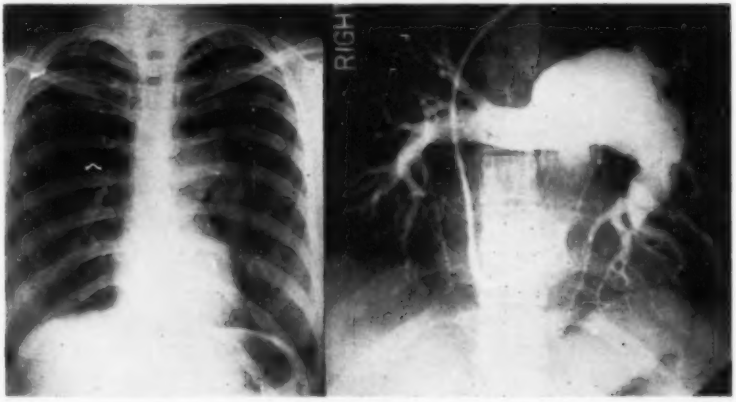

FIGURE 4: This 36 year-old woman with a large left hilar mass was thought to have a lymphoma, but angiocardiography and catheterization data established a diagnosis of pulmonary infundibular stenosis and post-stenotic dilatation of the left pulmonary artery.

Case Number	Age	Sex	Pre Angio Diagnosis	Location of Mass	Final Diagnosis	Bronchoscopic Findings	Unusual Features
1	73	M	Bronchogenic Carcinoma	L. Hilum	Dilatation of Pulmonary Artery Emphysema Cor Pulmonale Bronchiectasis, Lower Lobes	Negative	Pt. Developed Congestive Heart Failure and Died Necropsy Revealed a Diluted but Otherwise Normal Pulmonary Artery Chromogenic Acid-fast Organism Culture from Sputum
2	65	M	Bronchogenic Carcinoma TB Pneumonia Aortic Aneurysm	Bilateral	Pulmonary Artery Aneurysm	Negative	Cough, and Severe Hemoptysis
3	64	M	Bronchogenic Arteriosclerotic Heart Disease Fracture of Left Hip	L. Hilum	Distortion of the Left Pulmonary Artery Secondary To Resection of Left Upper Lobe for Chronic Inflammation	Negative	Peculiar Twist of Left Pulmonary Artery Seen in Lateral Angiogram Accounts for Mass in Left Hilus
4	74	M	Bronchogenic Carcinoma Rheumatic Heart Disease	Rt. Lower Lobe	Mitral Stenosis Dilated Pulmonary Artery	Extrinsic Mass Anterior to Rt. Main Bronchus Causing Narrowing of RMB and Compression of RL & RM Lobe Bronchi: Two Whitish Areas Biopsied	Repeat Bronchoscopy after Angiogram (and When Compensated) Reported Negative. Biopsy Negative
5	83	M	Atelectasis of Rt. Upper Lobe Tumor Mass in Rt. Hilum Arteriosclerotic Heart Disease	Rt. Hilum	Elevated and Dilated Right Pulmonary Artery Chronic Inflammation, Rt. Upper Lobe	Abnormal Orifice of Rt. Main Bronchus with Obstruction of Rt. Upper Lobe and Rt. Main Bronchi	Biopsy—Chronic Bronchitis
6	52	F	Carcinoma of Lung TB Rheumatic Heart Disease	Bilateral with Effusions Pleural	Constrictive Pericarditis with Displaced, Distorted Pulmonary Arteries	Negative	Protracted History of Pleural Effusions without Satisfactory Diagnosis
7	36	F	Bronchogenic Carcinoma	L. Hilum	Post-stenotic Dilatation of Pulmonary Artery	Not Done	Asymptomatic Minimal Heart Murmur
8	19	M	Rt. Hilar Tumor Found to Be Pulmonary Artery at Thoracotomy	Rt. Hilum	Eisenmenger's Complex Pulmonary Artery Aneurysm	Negative	Pt. Underwent Thoracotomy at Another Hospital Because of Strong Suspicion of Tumor in Spite of History of Heart Murmur and Cyanosis. Underlying Disease Not Diagnosed Until Cardiac Catheterization
9	34	F	Lymphoma Rheumatic Heart Disease	L. Hilum Tumor	Idiopathic Pulmonary Artery Dilatation	Not Done	Given Short Course of Radiation Therapy to Hilar Region
10	22	M	Rheumatic Heart Disease Lymphoma	Both Hila	Tetralogy of Fallot	Not Done	
11	54	M	Bronchogenic Carcinoma Arteriosclerotic Heart Disease	L. Hilum	Dilatation of Left Pulmonary Artery Arteriosclerotic Heart Disease	Negative	Readmitted in Congestive Failure and Again Mistakenly Diagnosed Bronchogenic Carcinoma

of the wall." Two of our cases (2 and 8 fit this diagnosis, but are still alive). The necropsy cases (1 and 6) are definitely not pulmonary artery aneurysms.

The widespread use of survey x-ray films as a method of early detection of intrathoracic pathology carries with it the obligation to separate significant disease which is neoplastic in origin and requires surgery from vascular shadows which are best left unmolested. If the possibility of dilated pulmonary artery is kept in mind, mistakes in this differentiation will be minimized. When there is serious doubt about the nature of the mediastinal hilar mass, angiocardiography should be done. No chest diagnostic service is complete without angiocardiographic facilities.

Case 1: This 73 year-old white man gave a three month history of cough and hemoptysis. An x-ray film by his private physician resulted in a diagnosis of bronchogenic carcinoma. The electrocardiogram showed a right ventricular hypertrophy pattern. X-ray films of the chest revealed a mass in the left hilar area. Venous angiocardiography revealed a dilated left pulmonary artery as the cause of the mass. A postmortem examination one year after angiocardiography revealed a normal appearing pulmonary artery, evidence of arteriosclerotic heart disease, and chronic bronchiectasis in the apex of the lower lobe of the left lung.

Case 2: This 65 year-old Negro presented with a one year history of cough and hemoptysis. Physical examination revealed a diastolic shock over the left pericardium and a sharply accentuated second pulmonic tone. The electrocardiogram showed a left ventricular strain pattern. The x-ray film of the chest showed a large mediastinal mass with an infiltration extending into the left lung. The venous angiocardiography revealed a large dilatation of the pulmonary artery, which was thought to be an aneurysm.

Case 3: This 64 year-old white man sustained a fracture of the right hip and was admitted in congestive heart failure. Two years earlier, he underwent a resection of the left upper lobe for a lung abscess. Physical examination revealed a left posterior thoracotomy scar, rales in the right base, and signs of congestive heart failure. The electrocardiogram showed a right ventricular hypertrophy pattern. The bronchoscopy was negative. The chest x-ray film revealed a well-defined mass in the left hilar region. Venous angiocardiography revealed an elevated, twisted, left upper lobe artery.

Case 4: This 74 year-old man had rheumatic fever in childhood and was admitted in congestive heart failure. Cardiac examination revealed cardiomegaly with a grade IV systolic apical murmur, a grade II early diastolic murmur at the aortic area, and signs of congestive failure. The electrocardiogram revealed a right bundle branch block. The chest x-ray film revealed cardiomegaly and a mass in the right lower mediastinal region which was thought to be carcinoma. Bronchoscopy revealed an extrinsic mass causing narrowing of the right mian bronchus from the anterior

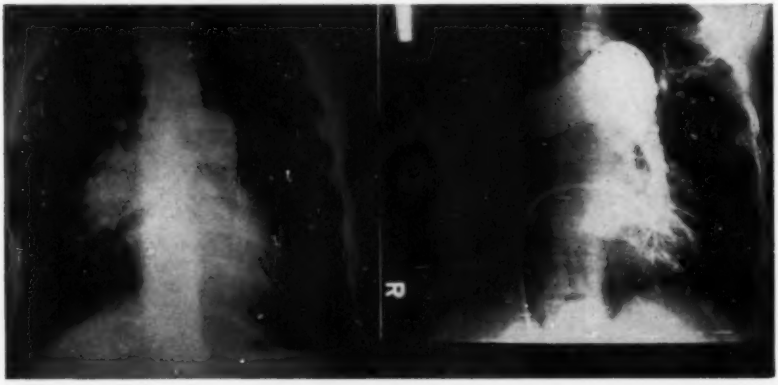

FIGURE 5: This 19 year-old man was found to have a mass in the right lower hilar area on a school survey film. He underwent thoracotomy with a preoperative diagnosis of pulmonary neoplasm and was found to have a vascular lesion. After surgery, catheterization and angiocardiography revealed aneurysm of the right pulmonary artery that was filled with clot. He also had an Eisenmenger's complex with extreme pulmonary hypertension.

medial aspect. Several areas of epithelium were biopsied and were histologically normal. The venous angiocardiography revealed that the mass in the right lower lung field was pulmonary artery.

Case 5: This 83 year-old man gave a brief history of shortness of breath, cough and expectoration. Physical examination revealed that the trachea was deviated to the right and expiratory rhonchi were heard over both lung bases. The chest x-ray film showed an atelectasis of the right upper lobe and a mass in the right hilar region. Bronchoscopy revealed an extrinsic obstruction to the right upper lobe bronchus with partial obstruction of the right main bronchus. A biopsy from the area of obstruction revealed mild chronic bronchitis. Venous angiocardiography revealed that the mass was an elevated right pulmonary artery.

Case 6: This 52 year-old housewife experienced rheumatic fever in childhood. Nine months prior to examination she began to experience severe chest pain radiation down the left shoulder and into the back. The patient developed bilateral effusions and had repeated thoracenteses which revealed bloody fluid negative for neoplastic cells. The electrocardiogram showed auricular fibrillation with nonspecific T wave changes. The scalene lymph node biopsy and lupus erythematosus preparations were negative. Cardiac catheterization and angiocardiography revealed that she had constrictive pericarditis as the cause for the bilateral pleural effusions. However, she succumbed and a necropsy proved this diagnosis to be correct.

Case 7: This 36 year-old woman complained of cough productive of yellow bloody material for seven weeks. She had diminished breath sounds and rales over the left lower lung field. A soft systolic murmur was heard at the cardiac apex. The chest x-ray film revealed a large left hilar mass with narrowing of the left main stem bronchus. The electrocardiogram showed right ventricular hypertrophy. She was thought to have a lymphoma with compression of the left main bronchus. The angiocardiography revealed a pulmonary infundibular stenosis with post-stenotic dilatation of the left pulmonary artery.

Case 8: A 19 year-old man was known to have congenital heart disease since early childhood. A routine school x-ray film survey revealed a shadow protruding from the right hilar region. Bronchoscopy was reported as negative. He underwent exploratory thoracotomy and the mass was found to be vascular in nature. After two unsuccessful attempts at cardiac catheterization, successful passage of the catheter to the pulmonary artery was obtained and selective angiocardiography revealed that the mass was a pulmonary artery aneurysm. The analysis of the catheterization findings resulted in a diagnosis of Eisenmenger's complex with a severe degree of pulmonary hypertension.

Case 9: A 34 year-old Negress with a lifelong history of asthma was found to have an abnormal cardiac silhouette on an x-ray film survey. The film showed an enlargement in the left hilar region and a diagnosis of lymphoma was made. She was given x-ray treatment over the left hilar region. There was no change in the size of the lesion after x-ray therapy, so she was referred for right heart catheterization and angiocardiography, which revealed the mass to be a dilated pulmonary artery (idiopathic).

Case 10: This 22 year-old white laborer complained of mild dyspnea on severe exertion for several years. Just prior to examination, he experienced severe melena.

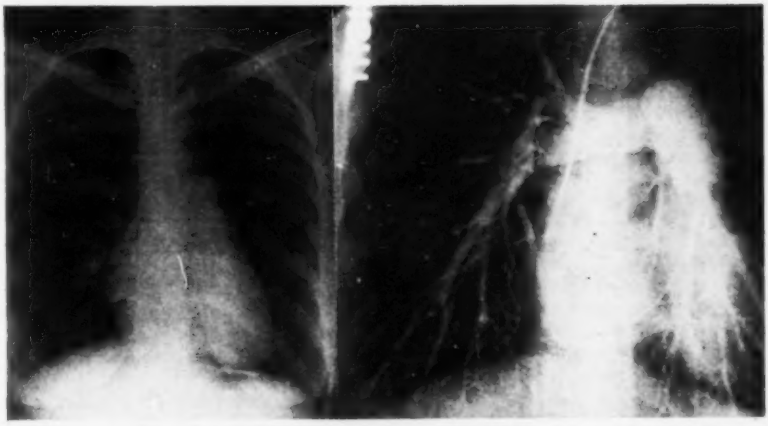

FIGURE 6: This 34 year-old woman was given radiation treatment to the left hilar area for what was thought to be a lymphoma. There was no response to radiation. The angiocardiogram demonstrated a dilated left pulmonary artery (idiopathic).

On examination, he was found to have pulmonary edema of moderate degree and frank melena. Cardiomegaly was present; a soft apical systolic murmur and accentuated pulmonary second sound were heard. Polycythemia and an abnormal electrocardiogram were noted. The chest x-ray film showed right and left hilar enlargement and a diagnosis of lymphoma was made. The angiocardiograms revealed an overriding aorta with large dilated pulmonary arteries.

Case 11: This 54 year-old laborer complained of dyspnea, cough, and left chest pain for one year. Physical examination revealed subcrepitant rales in the right posterior thorax. Chest x-ray film revealed a left hilar mass. The angiocardiogram showed the left hilar mass to be a dilated pulmonary artery.

SUMMARY

1. Eleven cases of abnormalities of the pulmonary artery are reported.
2. All 11 were mistakenly diagnosed as intrathoracic neoplasm.
3. One case was subjected to thoracotomy and one was given therapeutic radiation because of incorrect diagnosis.
4. Significant associated diseases contributing to pulmonary artery dilatation were reported in cases 1 through 6.
5. In cases 7 through 11, the abnormality was confined to the pulmonary artery and the lung fields were normal.
6. The role of angiocardiography in the diagnosis of abnormal hilar shadows is emphasized.

RESUMEN

1. Se relatan once casos de anormalidades de la arteria pulmonar.
2. Todos los 11 casos se tomaron erróneamente como neoplasias de torax.
3. Un caso sufrió toracotomía y en uno se dió terápia de radiación con motivo del diagnóstico equivocado.
4. Se refieren las enfermedades asociadas que contribuyeron a la dilatación de la arteria pulmonar en los casos del 1 al 6.
5. En los casos del 7 al 11 la anormalidad se limitó a la arteria pulmónar y los campos pulmonares eran normales.
6. El papel de la angiocardiografía de las sombras anormales del hilio se recalca.

ZUSAMMENFASSUNG

1. Es wird über 11 Fälle von Anomalien der arteria pulm. berichtet.
2. Alle 11 Fälle waren irrtümlicherweiss als intrathorakale Neoplasmen diagnostiziert worden.
3. Ein Fall wurde einer Thorakotomie unterzogen, und ein Fall erhielt eine therapeutische Bestrahlung infolge unrichtiger Diagnose.
4. Wesentliche und zur Erweiterung der Pulmonalarterie beitragende Begleiterkrankungen wurden für die Fälle 1 bis einschliesslich 6 mitgeteilt.
5. Bei den Fällen 7 bis einschliesslich 11 war die Anomalie auf die Lungenarterie beschränkt und die Lungenfelder normal.
6. Die Rolle der Angiocardiografie für die Diagnose abnormer Hilusschatten wird hervorgehoben.

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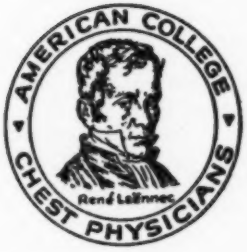

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NEW FORMAT FOR DISEASES OF THE CHEST

Beginning with the January issue, DISEASES OF THE CHEST will appear in a new format. An attractive green and black cover has been designed to replace the familiar blue binding. Text will appear in two columns, and a new type face has been selected for easier reading.

In addition to such features as the ROENTGENOGRAM and the ELECTROCARDIOGRAM OF THE MONTH, a new monthly section, PROGRESS IN CARDIOVASCULAR SURGERY, will be introduced.

The new format provides for earlier publication of worthwhile manuscripts. Foremost is our desire to maintain the highest possible standards found in a medical journal.

NEW COLLEGE BULLETIN

Meeting programs, chapter activities, council and committee reports, and other College announcements are always of special interest to our members. Until now, such items have been published in the College News Section of DISEASES OF THE CHEST; but, as space in the College journal is at a premium, the Editorial Board feels that it should be reserved for scientific material. To accommodate other items, a BULLETIN OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS will be published, the first issue to appear in January. All members of the College will receive this new publication.

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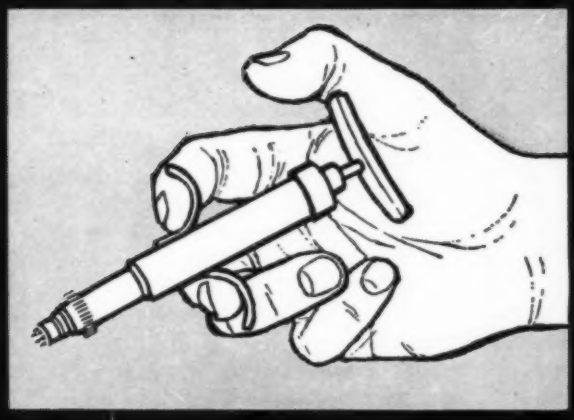

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